Tablet Splitting for Cost Containment

Introduction

Pharmaceutical manufacturers provide many medications in a variety of dosage strengths to facilitate titration of the appropriate dose to each patient. These different strengths of the same medication often have little or no price differential. For example, the 20 mg tablet and the 40 mg tablet of a particular drug may have the same price. By prescribing one-half tablet of the 40 mg strength instead of one full tablet of the 20 mg strength, the cost of the medication can be approximately halved.

In cases where patients are unable to afford their medication, physicians and pharmacists have sometimes worked together to enable the patient to obtain a higher dosage than is needed with a plan to cut the dosage forms in half. This approach can result in substantial cost savings for the patient.

However, this cost saving strategy is not always possible or appropriate. There are pitfalls with this approach that must be anticipated and avoided. Both the patient and the medication must be carefully chosen for the strategy to succeed.

The patient must be able to understand and implement the tablet splitting approach. Expecting the patient to be able to split tablets is unrealistic if the patient has:

- Cognitive impairment that limits the ability of the patient to understand and remember instructions for tablet splitting
- Arthritis or other impairment of manual dexterity
- Parkinson's disease or other tremors
- Visual impairment

Tablet splitting is an extra step in the process of medication administration. To overcome this additional barrier, patients must be motivated to take their medication. The motivation and

desire of the patient to take the medication must be great enough to overcome the need to do the additional work of tablet splitting.

The medication must also be carefully chosen. Medications that are enteric coated or have sustained release formulations are generally not suitable for splitting prior to administration. Capsules can also not be split since the capsule contents cannot be precisely divided or properly contained after the split. Scored tablets are generally easier to split.

Another consideration is the stability of the medication when exposed to air. Medication stability is generally studied with intact tablets. The effect of exposing cut tablets to the environment, as when tablets are cut in half before the dosage is taken, is often unknown. Many medications decompose rapidly when exposed to air and/or moisture.

A final consideration is the therapeutic or toxic window for the medication. With some medications, dosages must be carefully titrated and maintained to prevent either adverse effects or therapeutic failure. Because splitting of tablets produces high variability of tablet fragment sizes, the practice would be inappropriate with narrow therapeutic index medications.

Physicians and pharmacists are aware of the limitations and risks associated with tablet splitting. This approach is generally pursued with carefully selected patients, weighing the risks of tablet splitting against the likelihood that the patient will be unable to afford therapy at all without this approach.

Tablet Splitting and Health Policy

In recent years, health care payers have begun to consider tablet splitting as a strategy to save money for their health plans or programs. These plans deny payment for lower strengths of certain medications, requiring the patient to obtain the higher strength and split the tablets. The patients most affected by these policies are children and the elderly, who often need the lower dosage.

Rather than encouraging careful patient selection for this cost containment strategy, health plans reverse the process. All patients are automatically included. Access to the lower strength dosage forms is either denied or requires completing a prior authorization where the physician must demonstrate that the patient is unable to comply with the tablet splitting requirement. These policies have been implemented without research to evaluate their impact on health outcomes of the populations served. As health policy, tablet splitting is especially unsuitable for Medicaid populations, where a high proportion is elderly, disabled, or functionally impaired.

Research on Tablet Splitting

Teng and colleagues conducted a study of 11 commonly split tablets and evaluated the resulting half-tablets for content uniformity.1 Eight of the 11 tablets, when split, failed to produce half-tablets that met a liberal adaptation of the content uniformity test for tablets from the United States Pharmacopeia. These half-tablets did not contain between 85% and 115% of the intended dosage. Notably, scoring of the tablet did not predict whether the tablet would pass or fail this test.

McDevitt and colleagues evaluated the accuracy of tablet splitting by healthy volunteers.2 Ninety-four volunteers each split 10 tablets of 25 mg of hydrochlorothiazide. The split tablets

were weighed with an analytical balance to determine accuracy of splitting. Of the split tablet portions, 41.3% deviated by more than 10% from ideal weight, and 12.4% of the portions deviated by more than 20%. After this experience, 77.2% of the subjects stated a willingness to pay more for a standard tablet of the lower strength.

Rosenberg and colleagues evaluated variability of tablet fragments dispensed by a pharmacy.3 In this study, 30 of 560 tablet fragments (5.4%) deviated by more than 15% from the ideal weight. This level of accuracy was higher than reported by McDevitt with healthy volunteers, but still represents a significant variation.

What Can Go Wrong with Tablet Splitting?

It is important to recognize the risks involved in tablet splitting. In each step of the medication use process, the potential exists for miscommunication, errors, and adverse outcomes.

- On the prescription order, a prescription written for 1/2 tablet might be misread as 1-2 tablets.
- If the original prescription was for a whole tablet and the physician told the patient to take one tablet, the patient might follow the doctor's original advice instead of the revised plan with splitting the tablets.
- The patient may assume his or her prescription tablets have already been split (when they have not been) and take whole tablets instead of splitting them.
- If the tablets were split before dispensing, the patient may split them again without realizing or remembering that they have been split already.
- Confusion can result when the patient gets the medication refilled and the pharmacy splits the tablets when they have not previously done so, or vice versa.
- Patients may forget that they need to split a particular medicine, or get confused and split the wrong medicine.
- Patients may split the tablets unevenly and experience adverse effects from an excessively high dosage or exacerbation of the disease from a dosage that is too low.
- When the unused portion of split tablets are returned to the prescription bottle, tablet fragments can continue to crumble or split off before they are eventually used.
- Patients may get tired of splitting tablets and just stop taking the medication.

Tablet Splitting—Considerations for the Pharmacist

When tablet splitting is under consideration as a strategy for cost containment by a health plan or program, it is essential to consider what role (if any) is expected of the pharmacist and the dispensing pharmacy. If the pharmacist is to have any involvement in tablet splitting, these are the questions that must be considered from the pharmacist's perspective:

- Is tablet splitting legal?
- Will the pharmacist's malpractice insurance provide coverage for the practice?
- Is tablet splitting consistent with good patient care?
- If the pharmacist actually splits the tablets, how will the compounding fee be paid?

Tablet splitting is considered compounding by the pharmacist. It involves customization of a prescription that goes beyond providing a commercially prepared product to the patient. It also involves extra time and effort beyond that required for a typical prescription.

Pharmacists can legally compound prescriptions, but certain limitations exist under Section 503A of the FDA Modernization Act of 1997. There is no problem if the pharmacist is splitting the lowest commercially available strength of a tablet to create a customized dose for a patient who needs less of the drug. However, if the pharmacist is splitting tablets to reproduce a dosage that is commercially available, this action could be interpreted as a violation of the federal statute which says: "A drug product may be compounded ... if the licensed pharmacist ... (D) does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product." (emphasis added)4

The question of whether malpractice insurance provides coverage for tablet splitting is related to the first question. Baker says:

"Most policies contain an exclusion similar to this: 'This policy does not apply to ... damages caused by your willful violation of a regulation or statute pertaining to the practice of pharmacy ... committed by you or with your knowledge or consent.'"

The pharmacist must also consider whether tablet splitting is consistent with good patient care. Is the patient a suitable candidate for tablet splitting? Does the patient understand the risks and is the patient willing to assume those risks? Is the medication suitable for splitting? The professional judgment of the pharmacist applies in the decision to split tablets for the patient or to dispense tablets that will need to be split by the patient.

Finally, what is the mechanism to compensate the pharmacist for compounding the prescription for the patient? Does the health plan provide a compounding fee as part of the tablet splitting strategy? If the patient is expected to split the tablets, will the health plan pay for a tablet cutter for the patient?

Conclusion

The American Society of Consultant Pharmacists has issued a position statement strongly opposing policies to deny payment for lower strengths of tablet dosage forms, or otherwise mandate splitting of tablets by patients.5 In an editorial in Pharmacy Today, Daniel A. Hussar, Remington Professor of Pharmacy at the Philadelphia College of Pharmacy, stated: "Tablet splitting for economic reasons is bad patient care and bad pharmacy practice."6

References

1. Teng J, Song CK, Williams RL, et al. Lack of medication dose uniformity in commonly split tablets. J Am Pharm Assoc. 2002;42:195-9.
2. McDevitt JT, Gurst AH, Chen Y. Accuracy of tablet splitting. Pharmacotherapy 1998;18(1):193-7.
3. Rosenberg JM, Nathan JP, Plakogiannis F. Weight variability of pharmacist-dispensed split tablets. J Am Pharm Assoc. 2002;42:200-5.
4. Baker KR. Pill splitting—Is it legal? Is it covered by malpractice insurance? Florida Pharmacy Today. April 2000, pp. 14-15.
5. ASCP Policy Statement on Mandatory Tablet Splitting for Cost Containment
6. Hussar DA. Tablet splitting games are bad patient care ... and bad pharmacy practice. Pharmacy Today. May 2000, p. 5.

Prepared by: Thomas R. Clark, RPh, MHS
Director of Professional Affairs
American Society of Consultant Pharmacists
August 2002

News

NEWS INDEX

- News Archive
- Press Releases & Statements
- RSS News Feed

Note:

These press releases and statements were accurate, in all material respects, at the time of their issuance. However, Johnson & Johnson and the operating companies assume no obligation to update, correct or otherwise modify any of this material. We recommend that you view the most recent press releases and statements in order to receive the most current information made available by Johnson & Johnson.

News / News Archive

Study Demonstrates Splitting Muscle Relaxant Could Result in Inconsistent Dosing and Unpredictable Relief for Back Pain Sufferers

Variability in Weight Ranges and Drug Content of Split Muscle Relaxant May Put Patients at Risk of Receiving Too Much/Too Little Medication

Fort Washington, PA (September 15, 2004) – A research study investigating the appropriateness of pill splitting suggests that back pain sufferers who divide a 10-mg tablet of the muscle relaxant cyclobenzaprine hydrochloride (HCl) in order to achieve a 5-mg dose may get anywhere from half to one-and-a-half times the amount of medicine they believe they are taking. This practice may either deprive them of the intended therapeutic benefit of the medication or expose them to unintended side effects such as drowsiness. The findings appear in the September/October issue of the *Journal of the American Pharmacists Association*.

Following reports that patients given a prescription for the only available 5 mg dose of cyclobenzaprine HCl (FLEXERIL® 5 mg) were being advised to split higher dose 10 mg tablets instead, researchers at the Ernest Mario School of Pharmacy at Rutgers, The State University of New Jersey, conducted a study to determine the level of weight variability of tablet fragments when the 10 mg tablets were split into halves with two commonly used devices – a tablet splitter and a kitchen knife.

"Ideally, an evenly split 10 mg tablet should have 100 percent of the half tablet weight and 5 mg of the medication," explained study investigator Thomas J. Cook, Ph.D., assistant professor, Department of Pharmaceutics at Rutgers. "In this study, the variance in estimated drug content due to uneven tablet splitting ranged anywhere from 50 to 150 percent of the ideal targets, meaning a patient would have no guarantee of consistently receiving the intended amount of medication throughout the course of therapy."

FLEXERIL® 5 mg is comparable in efficacy to the 10 mg strength, but has been shown to be significantly less sedating. Clinical research has demonstrated that doses of cyclobenzaprine lower than 5 mg are not effective for the treatment of acute painful muscle spasm of the back or neck.

"Cyclobenzaprine HCl 10 mg tablets are not designed for splitting (tablets studied were film coated and unscored), so there is an increased likelihood that they will split unevenly, crumble or shatter," according to Dr. Cook. "Splitting unscored tablets to yield partial doses of a medication can result in uneven splitting that may, in turn, lead

Archive

- Johnson & Johnson Pharmaceutical Research & Development, L.L.C., & Grunenthal GmbH to Initiate Phase III Trials of Novel Analgesic for Moderate-To-Severe Acute Pain (April 28, 2006)
- Johnson & Johnson Announces Dividend Increase of 13.6% (April 27, 2006)
- Johnson & Johnson to Participate in Morgan Stanley Conference (April 27, 2006)
- New Meter Can Help People with Diabetes See the Relationship Between Food and Blood Sugar Control (April 26, 2006)
- Two Million Patients Treated With The CYPHER® Sirolimus-Eluting Coronary Stent (April 26, 2006)
- Community Health Organizations Assemble in Washington, D.C., for Johnson & Johnson Community Health Care Event (April 24, 2006)
- More News

to dosing errors and variable efficacy and safety of the medication."

The National Association of Boards of Pharmacy adopted a resolution in 2001 opposing mandated tablet splitting, describing the practice as "potentially dangerous" and driven by monetary considerations rather than the patients' best interests. The American Pharmacists Association (APhA) and the American Medical Association (AMA) have also stated that they formally oppose mandatory tablet splitting, and the APhA 2003-2004 Strategic Directions Committee recently proposed a practice tool to help pharmacists evaluate the appropriateness of tablet splitting in certain patient or product scenarios. Published in the May/June issue of the *Journal of the American Pharmacists Association*, the tool is designed to help pharmacists decide whether tablet splitting is appropriate based on certain product characteristics (i.e., is the tablet scored) and patient characteristics such as an individual's dexterity, strength and visual acuity.

"These considerations and the results of the current study strongly suggest that generic cyclobenzaprine HCl 10 mg tablets should not be cut in half," added Dr. Cook.

About the Study

Dr. Cook, an assistant professor of Pharmaceutics and a licensed pharmacist, and two fourth-year Doctor of Pharmacy students at Rutgers' Ernest Mario School of Pharmacy, conducted the study, which evaluated the weight variability of 90 cyclobenzaprine HCl 10 mg tablets. Each of the three participants split a total of 30 tablets – 15 each with a commonly used tablet splitting device and a kitchen knife.

Prior to splitting, each whole tablet was weighed on a special scale and the weight was recorded. The participants practiced the splitting technique with each device with up to four tablets; the weights of which were not included in the analysis.

After each tablet was split, the individual fragment weights were measured and recorded. A theoretical half-fragment weight (THW) of each piece was used to calculate percent weight and drug content ranges from the average weight of the tablets for each trial.

McNeil Consumer & Specialty Pharmaceuticals, a division of McNeil-PPC, Inc., U.S. marketers of FLEXERIL® 5 mg tablets, sponsored the study.

About FLEXERIL® 5 mg

FLEXERIL® 5 mg should be used for relief of painful muscle spasm along with rest and physical therapy. It should only be used for short periods of time, usually two-three weeks.

FLEXERIL® 5 mg is a prescription medicine and should not be taken by patients who have had a recent heart attack or have heart disease. It should not be used by people with an overactive thyroid or who are currently or have recently used MAOIs. Use of FLEXERIL® 5 mg with MAOIs can result in serious health complications.

FLEXERIL® 5 mg may enhance the effects of alcohol and other medicines that work on the central nervous system. In clinical studies the most common side effects were drowsiness, dry mouth and fatigue. For more information about FLEXERIL® 5 mg, including full U.S. Prescribing Information, visit www.flexeril.info or call 1-888-440-7903.

Reference herein to Rutgers, The State University of New Jersey, the Ernest Mario School of Pharmacy or faculty members of these institutions is intended for identification only and does not constitute an express or implied endorsement or recommendation by the institutions or their agents.

# # #

The Seattle Times
seattletimes.com

Thursday, December 18, 2003, 12:00 a.m. Pacific

High-dosage pill splitting saves money, irks patients

By Kyung M. Song
Seattle Times staff reporter

The idea is simple: Use a pill cutter to split double-strength prescription medications and halve your drug costs.

Health insurers — exploiting peculiarities of drug pricing that make some large doses just as cheap as smaller ones — are increasingly urging patients to buy higher-strength tablets and taking half at a time.

Last month, Regence BlueShield sent notices to 45,000 customers in Washington offering free pill splitters to anyone who accepts a higher-strength prescription. The deal applies to Zoloft, Vioxx and four other Regence-approved drugs. Seattle's Group Health Cooperative has had a similar program for a decade and was one of the nation's first health plans to do so.

But some patients contend that pill splitting isn't as easy — or voluntary — as insurers claim. Cutting drugs in even doses can be tricky, particularly for those who are very old. And promoting half tablets could tempt penny-pinching patients to split other drugs that should always be taken whole.

Also, pharmacists worry that insurers might eventually make splitting some tablets mandatory, inconveniencing them and their patients. The American Medical Association and the American Pharmaceutical Association formally oppose mandatory tablet splitting.

Making double-strength pills last twice as long can save patients with insurance $20 or more in regular prescription co-pays. Uninsured patients or those with no prescription coverage, including many seniors on Medicare, can save even more.

"Sometimes, splitting the tablet makes the difference between being able to afford the medication or not," said Marc Mora, an internist and chair of Group Health's pharmacy and therapeutics committee.

Ironically, one reason why pharmaceutical companies charge equal prices for drugs of different strengths is so people needing larger doses won't try to scrimp by splitting or skipping pills, said Dr. Randall Stafford, assistant professor of medicine at Stanford University, who last year published a study showing that tablet splitting can be safe and economic for certain drugs.

Stafford said the compound ingredients in drugs cost relatively little compared to development, marketing and distribution costs. A 20-milligram pill costs nominally more to manufacture than a 10-milligram pill, he said.

Don Williams, a Group Health patient who has taken cholesterol-lowering medication for six years, argues that the co-op erred in approving at least one

Pill-splitting hazards

Done correctly, splitting prescription tablets can save you money. Done incorrectly, it can endanger your health. Many prescription drugs that aren't specifically recommended for splitting can be split. But some never should be cut. They include:

- Drugs that have coating for controlled release or to protect against moisture, such as long-acting painkillers.
- Drugs that require finely calibrated dosages, including anti-seizure medications and blood thinners.
- Very small pills that are difficult to split evenly.
- Drugs that come in non-tablet forms, such as capsules.
- Drugs that cost more for higher strengths, which would reduce potential savings.

particular drug for splitting.

Williams's doctor put him on 10 milligrams of Zocor for his cholesterol but wrote the prescription for 20-milligram tablets. When Williams asked his Group Health pharmacist about the discrepancy, he was handed a pill cutter and told to split the tablets.

"There was nothing voluntary about it," recalled Williams, who happens to be a non-practicing pharmacist and executive director of Washington's Board of Pharmacy.

Williams had trouble splitting the shield-shaped Zocor pills. Zocor is coated and does not have a scored line in the middle, both of which hindered cutting. Williams estimates the pill broke in unequal doses four of 10 times. Group Health has since changed Williams' cholesterol medication twice. He now takes full-size lovastatin, a cheaper drug Group Health now favors for all its high-cholesterol patients.

Jim Carlson, Group Health's director of clinical pharmacy services, said Williams had the right to ultimately reject a half-tablet drug. But Carlson conceded that Williams' pharmacist could have failed to give him that option explicitly.

"If a patient expressed concern, the pharmacist would engage in more conversation" about the benefits of splitting tablets, Carlson said. "But there is not specific scripting on how patients are counseled."

Group Health's Mora said he is aware of long-standing concerns about cutting pills in even doses, especially for children.

But Mora said Group Health promotes cutting tablets only when it can be done safely. The co-op has eight prescription drugs — all non-scored — approved for splitting and allows half tablets for any medication when it is deemed safe by a physician or a pharmacist.

Premera Blue Cross, Washington's largest health insurer, does not endorse half tablets. "We believe that's something that strictly should be left to the doctor and the patient," said Premera spokesman Chris Jarvis.

Pill splitting can reap big savings for insurers. Prescription drugs are the fastest-rising category of health-care expenditures in the United States, outpacing increases in spending on doctors, hospitals and nursing homes. In 2001, Americans spent $1.42 trillion on health care, $140 billion of that on prescription drugs.

Splitting tablets means insurers have to pay for refills half as often. Cholesterol-lowering drug Lipitor, which is the No. 1 prescribed medication for Regence customers, costs the same for a 40-milligram pill as a 20-milligram pill. Each Lipitor pill on average costs $3.64 wholesale, which is the price before negotiated discounts.

SuAnn Bond, Regence's assistant vice president of pharmacy services, said it's too soon to gauge the popularity of its half-tablet program. Bond said Regence could shave as much as $5 million annually off its prescription-drug claims if every eligible patient split pills.

That would be a small but still significant savings for Regence, which pays out more than $200 million a year for prescription drugs. Patients have split pills privately for years to stretch their money. But insurers were slower to embrace the practice even as they were aggressively pushing generic medications as cheaper alternatives to name-brand drugs.

"There is no one thing that's going to reverse" rising prescription costs, Bond said. "But we can do a number of different things together."

John Oftebro, owner of Kelley-Ross Pharmacy in downtown Seattle, estimates that just about every other patient who lacks prescription coverage inquires about tablet splitting. Oftebro said many drugs, such as the anti-anxiety pill Valium or painkiller Vicodin, are meant to be split when patients don't need the full dose.

But Oftebro, a pharmacist for 38 years, warned that a host of drugs should never be split. They include medication with controlled-release coating, such as painkiller OxyContin, because breaching the coating could result in overdose. Other drugs, such as blood thinner Coumadin and anti-seizure medicine Depakote, can become dangerous if the dosage is off by even a milligram.

Oftebro worries especially about older patients who lack the dexterity to properly split very small or irregularly shaped pills.

Williams, the pharmacist who had to split his cholesterol medication, does not believe his treatment was compromised. Nonetheless, he remains unhappy that his Group Health pharmacist never gave him the option to take a whole pill.

"My feeling was that I didn't have any choice, and I was having to do this just to save them money," Williams said.

Kyung Song: 206-464-2423 or ksong@seattletimes.com

Defecetive Drugs: adrugrecall.com

CONSUMER-DRUG-SAFETY

- Safe-medication-use
- Counterfeit-medication
- Drug-safety
- Splitting-medication
- Drug-interaction
- Medication-samples
- Generic-drugs
- Online-medication
- Safety-seniors
- Fda-medwatch
- Medication-faq
- Reduce-error
- Tort-reform

Monday 2nd July 2007

Dangers of Splitting Medications

What is a generic drug?

Many consumers have resorted to splitting their medications in half to save money on prescription drugs. A number of insurance companies have even started promoting this controversial practice in an effort to reduce their costs. *However, no studies have been conducted to confirm the safety of this practice.* In fact, many in the medical community, including the ***American Medical Association*** , the ***American Pharmaceutical Association*** , and the ***American Society of Consultant Pharmacists*** , ***strongly oppose pill-splitting policies.***

Risk of Dosing Errors

Pill splitting involves a number of risks. Those who promote the practice often omit how splitting medications negatively impacts patient safety by ***increasing dosing errors*** . Many pills cannot be split, and those that can be split do not necessarily guarantee the proper dose.

Tablets often break or crumble unevenly, and even tablets with scores (a small groove down the center) don't always split evenly - potentially leading to situations where patients either ***under- or over-dose*** on their medications.

Pills That Should *Never* Be Split

There are multiple types of medications that should never be split due to an increased potential for dosing errors. These include:

- **Capsules** - These may contain a liquid, powder, or tiny pellets, which when cut open, cannot be divided equally.
- **Time-released medicines - These may also be called long-acting, controlled-release, or extended-release medicines. Splitting one of these pills is dangerous since it would cause a patient to receive several hours worth of medication all at once.**
- **Enteric-coated medicines - These types of pills release medicine after it has passed through the stomach. Splitting these pills may release the medicine too soon and cause stomach irritation or reduce the drug's effectiveness.**
- **Transdermal patches - Some patches contain a liquid or gel inside, which if cut would either release the drug too quickly or reduce the amount of medication transmitted. Also, the patch may not stick to the skin as well if it has been cut.**

Seniors at Risk

A research study published in the Journal of the American Medical Association found that tablets split by elderly patients resulted in a dose that *deviated between 9 and 37 percent from the intended dose* . Elderly patients are more likely to split pills because they tend to have a disproportionately lower income and thus split their medications to save money. Unfortunately, they are also more prone to make errors in the process because of unsteady hands or their increased risk for poor vision, arthritis, and other medical problems.

Splitting pills may save money in the short-term, but could end up costing more in the long-term if a medication error occurs. *It is always wise to consult with a physician when it comes to medication and proper dosing.*

For more on Consumer Drug Safety click here.

More Consumer-drug-safety Resources

CONSUMER-DRUG-SAFETY IN THE NEWS

More Issues

- Plavix Side Effects
- Fosamax Side Effects
- Trasylol and Aspirin
- Viagra Blindness
- Ortho Evra Attorneys

2nd Quarter 2000

National Pharmacy

IOM Report Addresses Medical Errors

A report released in late 1999 by the Institute of Medicine (IOM) of the National Academy of Science's Committee on Quality of Health Care in America concluded that rigorous changes throughout the health care system, including mandatory reporting requirements, are necessary to reduce medical errors and create a safer health care system.

Citing recent studies that place mortality estimates from medical errors between 44,000 and 98,000 annually, the Committee outlined a plan for government, industry, consumers, and health providers to reduce medical errors; called on Congress to form a national patient safety center to develop new systems that can address persistent problems; and set as a minimum goal a 50% reduction in errors over the next five years.

"Our recommendations are intended to encourage the health care system to take the actions necessary to improve safety," said William Richardson, chief executive officer of the W.K. Kellogg Foundation, Battle Creek, Mich, and chair of the Committee. "We must have a health care system that makes it easy to do things right, and hard to do them wrong."

The report, entitled "To Err Is Human: Building a Safer Health System," is available for a fee by calling 800/624-6242. The IOM is a private, nonprofit institution that provides health policy advice under a congressional charter granted to the National Academy of Sciences.

FDA Issues Final Dietary Supplement Labeling Rules

In the January 6, 2000 *Federal Register*, the US Food and Drug Administration (FDA) published final regulations that define the types of statements that can be made concerning the effects a dietary supplement has on the structure and function of the human body pursuant to the Dietary Supplement Health and Education Act of 1994 (DSHEA). The regulations are intended to clarify the types of claims that may be made for dietary supplements without prior review by the FDA, as well as the types of claims that require prior authorization through the establishment of criteria for determining when a statement about a dietary supplement is a disease claim.

Under DSHEA, dietary supplements may, without prior FDA review, carry "structure/function" claims (ie, claims that a product may affect the structure or function of the body), but may not, without prior FDA review, carry express or implied claims that they can treat, diagnose, cure, or prevent disease (disease claims). For example, the express disease claim "prevents osteoporosis" and the implied disease claim "prevents bone fragility in postmenopausal women" would be prohibited without prior FDA review. The rule clarifies that express and implied disease claims made through the name of the product (ie, Carpaltum, CircuCure); through a statement about the formulation of a product (ie, contains aspirin); or thorough the use of pictures, vignettes, or symbols (ie, electrocardiogram tracings) can be made. It also permits claims that do not relate to disease, such as health maintenance claims ("maintains a healthy circulatory system"); other non-disease claims ("for muscle enhancement"); and claims made for common, minor symptoms associated with life stages ("for common symptoms of PMS," "for hot flashes").

Under DSHEA and existing regulations, dietary supplement manufacturers are already required to maintain documentation substantiating structure/function claims and must include a disclaimer on their labels that their products are not drugs and receive no FDA pre-market approval. They must also notify the FDA of the claims they are making within 30 days of marketing.

The final rule became effective February 7, 2000. For further information contact Ann Marlin Witt, Office of Policy, Planning, and Legislation (HF-11), FDA, 5600 Fishers Lane, Rockville, MD 20857, 301/827-0084.

Tablet-Splitting Policies Raise Concern

Some state boards of pharmacy are concerned about the cost-saving initiatives of certain health care plans that encourage or mandate the practice of dispensing higher doses of certain medications so that patients must split the tablet to obtain the appropriate dose. Targeted are those high-cost drugs that are available in similarly priced higher- and lower-dose tablets, such as Zoloft®, which has 50 mg and 100 mg dosages selling for about the same price. Medical insurance plans favoring this method of cost cutting provide pill-cutters to enrollees and instruct physicians to prescribe the higher dosage tablets.

Inaccuracies in tablet splitting, the lack of testing on the effectiveness of split pills, and the potential for overdosing are the primary issues of concern. "As a cost-saving measure, tablet splitting may be considered in certain situations; however, health care insurers should not mandate such practices for financial gain without regard to patient safety," says NABP President Dyke F. Anderson. "The pharmacist is ultimately responsible for providing adequate patient counseling, and for assuring that tablet-splitting is safe and appropriate for the patient."

FDA Targets Illegal Internet Prescription Sales

The US Food and Drug Administration (FDA) is furthering its efforts to combat illegal Internet prescription drug and device sales. The agency recently announced that it has issued, via the Internet, warning letters to a dozen foreign-based Internet

National Association of Boards of Pharmacy
700 Busse Highway • Park Ridge, IL 60068
Tel: 847/698-6227 • Fax: 847/698-0124
Web Site: www.nabp.net

RESOLUTION NO. 97-4-01

TITLE: **Opposition to Mandated Tablet Splitting**

Whereas, insurance companies and pharmacy benefit managers are advocating and mandating that practitioners prescribe and pharmacists dispense dosages of medications that may require the patient to physically split the medication; and

Whereas, the precise splitting of tablets may be difficult for patients, resulting in under- or overdosing and endangering patients' health; and

Whereas, the tablet splitting practices advocated and mandated by insurance companies and pharmacy benefit managers do not appear to be in the best interest of the patient but, rather, monetarily driven;

THEREFORE BE IT RESOLVED that NABP oppose this mandate by working with other national associations and government agencies to stop this potentially dangerous practice.

(Resolution passed at NABP's 97th Annual Meeting, Seattle, WA)

"Pill Fragmenting Program" -

Presentation by Charles Phillips, MD of Fresno, California
On Invitation to Speak at the California Board of Pharmacy
San Diego Meeting on January 31, 2007

INTRODUCTION

I would like to thank the Pharmacy Board's Subcommittee on Medicare Drug Benefits Plan for inviting me,[1] a physician, to discuss pill fragmentation before the full Board today. It is appropriate that this presentation be in San Diego for it is here that pill splitting got its start [2] and, perhaps, where it should as massive programs be stopped.

I also have to thank Maggie Dee for helping me to understand this problem through the disabled patient point of view as well. One patient she helped me to meet by Email is Mr. Nick Feldman, who due to cerebral palsy can only move his head. Yet he has graduated from UC Berkeley. He has been forced by Kaiser to split pills – Zanaflex 4 mg into two pieces that are supposed to simulate the 2 mg tablet. He saw the fragments created by his attendant's best efforts and stopped the splitting. He takes the whole dose in the morning to avoid the humiliation of medication fragmenting. This means he is over sedated in the morning and has muscle cramps in the afternoon. He has asked – through an Email to me – that you listen to me today and take action soon; he knows what is going on and wants it to be stopped.[3]

I believe large scale "pill splitting" to be a form of general patient abuse; it is particularly obnoxious to force onto the disabled. It is a form of **senior abuse.**[4] It is also - in its

---

[1] My friends would find me well qualified to talk about HMOs and medications – as I have written a whole chapter of one of my textbooks on "Medication Administration" [Exhibit #1]. I have taught the same topic to nurses and paramedics as well. My enemies would try to destroy me as a messenger by pointing to a tattoo on my medical license around not catching a physician assistant's poor evaluation on a child in 1999. Luckily all peer reviews of that incident have been in my favor, and I never lost being Board Certified in Emergency Medicine – now for my 25th year.

[2] Pill splitting began with Dr. Anthony Morreale at the VA in San Diego. Later he became the "Pharmacist Benefit Manager" for VISN 22 – the whole West Coast as pill splitting spread to the VA in Long Beach. Then it spread to Kaiser through Dr. Fawell who moved from the VA in Long Beach to Kaiser Vallejo. The VA has conceded that the pills split unevenly. Thus many have the vets split one pill every two days so that big and little fragments might be matched up (e.g. Tampa, Florida VA).

[3] One of the tricks used by Kaiser is to use two formularies – one for outpatient care that shows only one size for many medications – like Zanaflex 4 mg, Maxzide full strength, etc. The other one is seen by very few eyes but is built into the in-hospital dispensing systems with variable doses so that nurses are almost never asked to split pills. Zanaflex 2 mg is available in the Kaiser Hospitals. The traveling nurses – with no dental benefits – would be the first to turn Kaiser in for pill chopping if it occurred in the hospital. So if it is not safe for a nurse, how does that make it safe for a patient?

[4] Naturally, I do not object to the few cases where pill splitting is necessary – titration on the way to the correct dose, getting a patient through a weekend when a pharmacy is out of a medication, or helping a

HMO form - the illegal corporate practice of medicine by the top hierarchy[5] of the for-profit physician partnership[6] called the Permanente Federation.

Pill fragmentation or chopping results in **uneven fragments producing uneven treatment**.[7] In the case of the Kaiser HMO called "Kaiser Permanente"[8] this puts the risk of accelerating cardiovascular and depression illnesses onto the patients – opposite to the $45 million a year ad campaign with its "Thrive" message [Exhibit #4]. And nowhere in Kaiser's ads or website are seniors – the most vulnerable - warned that they might be funneled[9] into pill splitting schemes or just what uneven pill fragments mean.

---

patient (like a child) achieve a correct medication dosage where there is no manufactured alternative. Pill scores were never meant to be invitations for massive pill fragmentation and is not condoned by the manufacturers, the FDA, the surgeon general, CMS, the AMA, pharmaceutical malpractice insurers, and many others.

In fact, the California Medical Board did vote with the other medical boards [the National Association of Boards of Pharmacy (NABP) in Seattle in No. 97-4-01 voted on in 1998 – "Whereas, insurance companies and pharmacy benefit managers are advocating and mandating that practitioners prescribe and pharmacists dispense dosages of medications that may require the patient to physically split the medications … [programs that are] monetarily driven; therefore it be resolved that NABP oppose this mandate by working with] other national associations and government agencies to stop this potentially dangerous practice" [See Exhibit #2]

[5] Kaiser HMO, its hospitals, and the very profitable Permanente Medical Groups (the Federation) are run out of the Ordway building [pictured in Exhibit #3] – Mr. George Halverson and Dr. Francis Crosson being co-chairman of the top executive committee. They each have an office on the 27th floor – thus only a few doors down the hall from one another. They each hope to be aloof to these decisions that tie the hands of doctors at the frontline. Those physicians and pharmacisits who complain are deemed "not manage care suitable" and expelled. Many physicians don't even know that their prescriptions result in double doses and pill splitters – as a ER physician I did not catch on for one year. These decisions lead to the Sustainable Future of the partners – see the Permanente Map in the same Exhibit – not the patients. In fact, the unethical "group ethic" and the illegal "Permanente-patient relationship" are included on the greed map. This is "corporateering" at its worst.

[6] As the HMO Act of 1973 created federal enhancement of prepaid health plans like Kaiser (the mother or grandfather of HMOs), it also required "independent physician groups" be put at financial risk. Such IPAs – like the Permanente group – do take risk for profit but pass that risk on to patients as rationed and often dangerous care. The patient caries the risk of illness; the physician carries the likelihood of profit – million dollar plus pension plans creating $15,000 a month as the MDs turn senior.

[7] In fact, the topic should never be called "pill halving" [which rarely occurs] or even "pill splitting" [still sounds sort of even], but rather **pill fragmentation,** which is really what happens.

[8] The Kaiser lawyers are the first to point out that "Kaiser Permanente" does not exist as a legal entity. There are only three organizations who use a common strategy of care.

[9] I use the word funneling because Kaiser can achieve 98% uniformity of prescription for hypertension, diabetes, high cholesterol, etc. using the following tools: pocket reminders, EPIC program computer pop - ups, peer pressure, medication utilization tracking, pay check reminders, one on one talks, our-way-or-the-highway, etc. And the funneling is toward split pills – Tolinase, lisinopril, statin of the year, Paxil, Zoloft, Maxide, etc. The physician has little choice, so the patient has little choice. Pharmacists who complain are not encouraged to stay.

Time for Transparency

Transparency in health care is the only way to give back to seniors what has been so often stolen from them – the true information on which to base real consent. There can never be "informed consent" without the person being first fully informed.

And as this month is part of the-health-plan-switching period of time in Medicare, this is a good time for extra honesty. Either pill fragmenting is a way for the world to save $15 billion in pharmaceutical expense or a way to cost patients some $60 billion in early illness from uneven dosing.[10]

I originally sent you a formal complaint in 1998 - (#C1-98-17552). The silence of the previous Pharmacy Boards up until now – except for a quiet vote in Seattle [Exhibit #2] – has made the previous boards co-enablers of pill fragmenting in California. I ask that you transform your vote in Seattle to action in California. Further silence will simply endorse the status quo – massive pill splitting by the uniformed.

The Weighing Data

Is this "pill halving" or is it "pill fragmenting." The classic study of J.T. McDevitt in 1998 published in Pharmacotherapy [Exhibit #5] is quoted both by Kaiser and the VA as well as all experts on the topic of pill fragmenting. No one has ever proved him wrong. And these were volunteers from a newspaper ad, not sick patients.

Exactly 1752 pills were split by 94 healthy volunteers, the latter recruited from a newspaper ad. "Some 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%." Amazingly it did not matter if the pill had a score line or if the pill was split by hand or a pill splitter from Rite-Aid[11]. "Given the choice, 96.8% of volunteers stated that they would rather not split a tablet if a lower-dose formulation was available."

And what we find in the general practice of pill splitting is that dependent patients are compliant with the general funneling system toward one product. But they are uniformed of true risks. White coats give patients the impression that it is perfectly safe. The very labels used by the HMOs – Kaiser and United HealthCare[12] of the "Pill Halving" programs is 100% deceptive since halfs are not produced.

The VA has tried some weighing experiments even using a trained pharmacy student, and still the fragments were often greater than 10 percent of the hope for a half weight. In that study, the article suggested that lisinopril not be split; Kaiser does still split it. Those

---

[10] Since most strokes are often sent home after Kaiser ER evaluation, the cost of care falls back to the family and not to the HMO.

[11] Rite Aid, Walmart, Walgreens, private pharmacists, Stanford, Harvard, Yale, etc. are not into pill fragmentation. It takes a dependent population who have prepaid benefits, a difficult path for legal suit, and the co-enabling by government - to pull of pill fragmentation.

[12] Dr. William W. McGuire who helped to okay pill splitting at United GroupHealth received an average compensation of $57,843,000 per year for his last six years.

VA areas with at least partial ethics had their patients split pills every other day – so big pieces would be matched with small pieces. They did not mention this in most of their articles; and Kaiser leans on VA "research" as its backup.

No one has done this weighing study with seniors who have the usual co-morbidities of arthritis, hypertension, high cholesterol, acid reflux, and occasional depression. This weighing experiment could be done easily and quickly.

Seniors can be on three Kaiser splits at one time – like Mary O'Donnell of Corcoran California who has now passed away. A page from her medication diary [Exhibit #6] and Kaiser medication records show the splitting of her blood pressure pill, her anti-cholesterol pill, and her anti-depression pill[13] all at the same time.

Or what about Audrey Timmis, an oxygen dependent patient who was asked to split Maxzide. Kaiser did not even order the smaller, senior dose for their formulary – regular dyazide (capsule) or Maxzide-25 – because the national goal in Kaiser pharmacy procurement in the Oakland highrise [See Exhibit #3] was to set up massive pill splitting and no choice. It saved money to order millions of Maxzide pills and have them rebundled into 100 pill bottles in Livermore. That translated for Audrey to have pieces – she called "tiddley winks" – flying all over her kitchen, even with her husband helping.[14] For goals spelled out in Kaiser-eeze in the Recovery Plan by 2001 – Audrey did not matter; profit mattered.

Kaiser's top profit year was 2004; the profit was $2 billion – half going to the physicians. And pill fragmenting contributed to the profit. That is blood money in my book. How many strokes and heart attacks we will never know – the evidence is swallowed. It is almost the perfect crime. But it lacks professional ethics. And that is why we have professional boards – to foster ethics and protect patients.

Am I Alone?

I am sometimes viewed as a Lone Ranger type in health care. However, my position against pill splitting is supported by:

1. the manufacturers [letter available from Merck];
2. the FDA safety committee;

---

[13] By the way, I was in Mary O'Donnel's house the day ABC News investigated pill splitting. She never felt she had Informed Consent or any choice. She was part of the law suit against Kaiser whereby after Kaiser's $1 million plus defense effort, the judges ruled that Kaiser was right – this issue belongs before the California Board of Pharmacy and the California Department of Managed Health Care. In fact, your ongoing "investigation" became their defense that they should not have to defend the same issue on more than one "front." They also admitted what I have long maintained, that "Kaiser Permanente" really does not exist. Kaiser maintains that they won this suit were embarrassed into dropping their splits from thirty-eight before the suit - including heart rhythm medication and seizure medication – down to about ten.

[14] Another reliable patient has called these type of pieces "grenade fragments."

3. the American Society of Pharmacy Consultants – same policy for years;
4. most malpractice carriers for pharmacists;
5. increasingly seniors who start to understand pharmacy science;
6. veterans who wonder why the VA has never declared splitting safe by their Technical Advisory Committee;

Those who are against large splitting programs coming down from those who would be less responsible – like "Medical Directors" of HMOs – include:

1. the Surgeon General;
2. the FDA;
3. the National Boards of Pharmacy in Seattle;
4. the American Medical Association;
5. most of the physicians and pharmacists on the frontline of Kaiser who actually complement me privately for reducing the corporate pressure coming down from Oakland.[15]

Those who seem to like splitting include:

1. Top MDs and administrators at HMOs like Kaiser and United HealthCare with a focus on seniors (and great retirement programs for top management);
2. the VA regional programs who compete with each other for limited funds – really a federal HMO the same size as Kaiser;
3. "Pharmacy Benefit Managers" like those in Wisconsin and Michigan;
4. the "outcome centers" supported by the federal government and often a Kaiser Family endowed chair – like Stanford; though Stanford pharmacists have not joined this practice;
5. Medicaid wherever Pharmacy Boards are lax;
6. some newspapers who think that medications cost to much and do not have an independent pharmacist on staff to really explain the risk vs. benefit of uneven dosing;
7. pill splitter companies.

I admire those pharmacists in Kaiser who split the pills for the patients who need half pills because of no available size on the market – as in pediatrics. I do not admire those physicians and pharmacists who have decided to go along with this approach so as to achieve personal "vesting" goals for golden retirements. One group of future seniors should not get to the Golden Pond on the pain and suffering of other seniors.

---

[15] One ex-Kaiser pharmacist might be willing to privately testify to a Board investigator. But the risk of going against Kaiser is to have one's career ruined. As with "The Firm," getting out of Kaiser without being damaged on the way out is very difficult. Those out of Kaiser can also be damaged by sympathetic IPAs and hospital "risk management" offices that can change alter medical records without a flit of conscience.

Kaiser would easily spend $5 million wining and dining all of the politicians possibly involved up through the Governor[16] to keep pill fragmentation programs humming along and to cast me as an outlier. Usually physicians like me are pictured as eagles soaring over the canyons of the past (like Dr. Welby) who had no real sense to know that it is either HMO medicine [called "private health plans"] or government medicine.

I hope to hear of the new investigations that this presentation should set off. But either way history will take note of what California allowed on each and every consumer board watch. And it will also conclude that a Board vote of each individual professional is as much a licensed decision as the handing over of a pill bottle [17] to a specific patient.

Conclusions

Of the two $35 billion a year budget organizations who split pills, the group over which you have authority to protect the public is Kaiser with 800,000 enrolled seniors[18] involved with Medicare D. As 75% of Kaiser has always been in California,[19] that is 600,000 vulnerable California seniors who will only learn about who "Thrives" when they get sick or need medication.

What is needed now by the Pharmacy Board is a rapid investigation that goes way beyond asking for another letter from Kaiser. It is time to show up unannounced at the frontlines of Kaiser care and to see what senior splits really look like. That means looking into the brown bags. Your eyes will tell you – as they did mine in 1998 – that there is no need to even have another weighing of fragments; this is really about pill destruction for high profit.

Too many many people are starting to call California "Kaiser-fornia." It is important that you do not let the tail wag the dog.

Don't take action for me. Do it for Maggie Dee, for Nick Feldman, and for the memory of Mary O'Donnell.

---

[16] The style is for the Kaiser Plan to give the Permanente Physicians money that is then sent on to the governor. Or one of his pet projects is enhanced – like health care built on the magnification of HMOs.

[17] I briefly worked in a job with the Hmong community of Fresno that gave me only one choice for a medical plan – Kaiser. I joined so as to be a patient witness to what they do and what kind of misery it is to call into the system. They also managed to print one of my prescriptions in Spanish. I know Kaiser both as a former

[18] This may be found in the internal, 2006, year end summary written by Mr. George Halverson, CEO, Chairman of the Board, and President of the Kaiser Plan, Inc., and Kaiser Hospitals, Inc. – both using the same board. Identical boards allow money to travel down from the Plan to the for profit doctors and the for bonus hospitals and then travel back up through the hospitals to become bonuses at the top.

[19] Kaiser has withdrawn from many states in its history – New York, New Jersey, North Carolina, Texas, Missouri, Utah, etc – and has not ventured into a new state since developing its money losing plan in Washington, DC where it bought into Humana as the latter left. The Missouri Kaiser attempt folded because it had to send $4 million excess each year to prop up the DC unit – see court papers.

And do it for the Class of 2010 (see inside of your notebook); don't let them graduate into a world of challenged ethics. The Hippocratic Oath is both a Oath and a Covenant invoking upon anyone who would misuse these talents misery in this life and the next.

1 My CV and Textbook

2 NABP Resolution Against Large Scale Pill Splitting

3 Kaiser CEO + Top Physician - and the Permanente Map

4 California - 49% HMO
Thrive Ads (Splitting Not mentioned)

5 McDevitt's Classic Study of Pill Fragmentation

6 Mary O'Donnel's Pill Diary - Three Splits at One Time

7 VA "SPOT" Harm Reports > 400

8 Nicholas Feldman and the Zanaflex fragments

1: Pharmacotherapy. 1998 Jan-Feb;18(1):193-7.

Accuracy of tablet splitting.

McDevitt JT, Gurny AM, Chen X.

MEDEX Clinical Trial Services, Inc., Ardmore, Pennsylvania 19003, USA.

We attempted to determine the accuracy of manually splitting hydrochlorothiazide tablets. Ninety-four healthy volunteers each split ten 25-mg hydrochlorothiazide tablets, which were then weighed using an analytical balance. Demographics, grip and pinch strength, digit circumference, and tablet-splitting experience were documented. Subjects were also surveyed regarding their willingness to pay a premium for commercially available, lower-dose tablets. Of 1752 manually split tablet portions, 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%. Gender, age, education, and tablet-splitting experience were not predictive of variability. Most subjects (96.8%) stated a preference for commercially produced, lower-dose tablets, and 77.2% were willing to pay more for them. For drugs with steep dose-response curves or narrow therapeutic windows, the differences we recorded could be clinically relevant.

PMID: 9469693 [PubMed - indexed for MEDLINE]

DRUG USE INSIGHTS

Accuracy of Tablet Splitting

Joseph T. McDevitt, B.S., Andrea H. Gurst, B.S.N., and Yinshuo Chen, Ph.D.

We attempted to determine the accuracy of manually splitting hydrochlorothiazide tablets. Ninety-four healthy volunteers each split ten 25-mg hydrochlorothiazide tablets, which were then weighed using an analytical balance. Demographics, grip and pinch strength, digit circumference, and tablet-splitting experience were documented. Subjects were also surveyed regarding their willingness to pay a premium for commercially available, lower-dose tablets. Of 1752 manually split tablet portions, 41.3% deviated from ideal weight by more than 10% and 12.4% deviated by more than 20%. Gender, age, education, and tablet-splitting experience were not predictive of variability. Most subjects (96.8%) stated a preference for commercially produced, lower-dose tablets, and 77.2% were willing to pay more for them. For drugs with steep dose-response curves or narrow therapeutic windows, the differences we recorded could be clinically relevant.
(Pharmacotherapy 1998;18(1):193–197)

Tablet splitting is a frequent method of obtaining the prescribed dose of a drug. Physicians prescribe doses depending on a patient's disease and level of drug tolerance; however, drugs do not always come in the appropriate strength, in which case tablets must be broken into portions. When patients are instructed to split tablets that are not intended to be split, the potential for dosing errors is introduced.

It is a violation of pharmacy law in most states for a pharmacist to dispense split tablets. Recognition that dosing flexibility is required to treat patients accurately led certain pharmaceutical manufacturers to introduce tablets specifically intended for splitting (Glynase PresTab, Upjohn, Kalamazoo, MI; Tagamet TiltTab, SmithKline Beecham, Philadelphia, PA; etc.).

Relatively few controlled studies have been performed to evaluate the accuracy of splitting tablets. In one study, 10-mm oval tablets scored on both sides had the least variability in weight between portions when broken manually.[1] Large round tablets that were scored on one side tended to break unevenly, with large variability in weight between sides. Small (7-mm) round tablets were the most difficult to break accurately, with 44% of portions deviating from ideal weight by more than 20%. In addition, active drug was lost due to fragmentation and powdering during splitting. Some tablets have a protective coating that interferes with splitting, and others are specifically not intended to be split (e.g., enteric-coated tablets). Use of a tablet-splitting device resulted in findings similar to manual splitting.[2]

Currently, the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure recommends that the lowest effective dosage of a diuretic or β-blocker be first-line therapy for hypertension after a trial of lifestyle modifications.[3] Hydrochlorothiazide is frequently prescribed in this circumstance. A large body of evidence suggests that a low dosage (12.5 mg/day) is both effective and safe,[4–11] but dosages of 6.25 mg/day were not consistently effective in controlling hypertension.[12–14] At 12.5 mg/day, blood pressure reductions are generally similar to those with 25 mg/day, although with

From MEDEX Clinical Trial Services, Inc., Ardmore, Pennsylvania (all authors).

Address reprint requests to Joseph T. McDevitt, MEDEX Clinical Trial Services, 10 East Athens Avenue, Ardmore, PA 19003.

fewer metabolic adverse effects. Increasing the dosage beyond 50 mg/day generally does not improve blood pressure control.

Until recently, the agent was available only as a relatively small (6-mm diameter), 25-mg, round, scored tablet. It was therefore necessary to split the tablet to approximate a 12.5-mg dose. A 12.5-mg formulation of the agent (Microzide capsules; Watson Laboratories, Corona, CA) has been approved for marketing in the United States.

Methods

Ninety-four volunteers were recruited from a suburban Philadelphia neighborhood through a newspaper advertisement. Adult men and women were eligible to participate without regard to race, religion, or socioeconomic background. Subjects reporting severe vision impairment, missing arms or digits, or disabling arthritis were excluded. Demographic and survey information was collected from each volunteer (Table 1, Figure 1).

Measurements

Each subject's grip strength was measured using a hydraulic hand dynamometer (JAMAR, Jackson, MI) before splitting. The subject sat with arms resting on a table and palms facing medially. The dynamometer was set at level 1 with the indicator at zero. The subject was instructed to squeeze the dynamometer as hard as possible using one hand and a slow, steady grip. This procedure was repeated 3 times for each hand, and the subject's mean grip strength was calculated.

Pinch strength was documented using a standard pinch test gauge (B&L Engineering, Santa Fe Springs, CA). The subject sat at a table with arms pronated. The indicator on the pinch test gauge was set to zero. The gauge was placed between the subject's thumb and distal phalanx of the index finger. The subject slowly compressed the pinch tester, and the maximum value was recorded. This procedure was repeated 3 times for each hand, and the subject's mean pinch strength was calculated.

The circumferences of the distal phalanges of the right and left index fingers were measured using a standard ring gauge. The ring that slid on and off the fingers easily, but allowed no additional room, was judged to be the appropriate size. The size of the thumb of each hand just above the first joint was measured and documented using the same procedure. Finally, the length of the subject's fingernails was noted. Long and short fingernails were defined as those that did and did not extend beyond the digit, respectively.

Table 1. Demographic Information

Variable	Mean (SD)	Range
Age (yrs)	42.6 (14.8)	20–77
Weight (kg)	74.38 (17.27)	45.4–136.2
M/F	39/55	
High school education (no.)	16	
College education (no.)	78	
Fingernail length	36 long, 58 short	
Tablet-splitting experience, yes/no (%)	35.1/64.9	

Splitting Test

Each subject was provided with 10 tablets of hydrochlorothiazide (HydroDIURIL; Merck & Co., West Point, PA) that were randomly selected from a commercial supply bottle. Each tablet was weighed in milligrams on an electronic scale (Sartorius, Goettingen, Germany) before splitting. This scale had a minimum sensitivity of 0.001 mg. Subjects sat with forearms resting on a table and were instructed to split each of the tablets evenly by grasping and applying pressure to each side of the tablet with the thumbs and forefingers. If successful, subjects placed the tablet fragments from their right and left hands into appropriately marked containers, and the two portions were weighed in milligrams. This sequence was repeated until each subject had divided all 10 tablets.

In the event that a subject was unable to apply enough pressure to break a tablet manually, he or she was allowed to follow the same procedure using a commerical tablet splitter (Rite-Aid). Subjects who began splitting tablets manually bu were unable to complete the process on all 1(tablets were allowed to divide the remainin tablets using the tablet splitter.

Statistical Analyses

Statistical tests of significance of preexistir conditions (age, gender, grip and finger pinc strength, finger size) on results of tablet splitti

1. Would you see a distinct benefit *not* to have to split tablets? (Yes/No)
2. Would you be willing to spend a little extra money f the convenience of not having to split tablets? (Yes/N
3. How much would you be willing to spend if a 1-mo prescription originally cost $5, $10, $20, $50?

Figure 1. Survey.

Table 2. Results of Manual Tablet Splitting

	No.	Mean (SD)	Range
Whole tablet weight (mg)	876	108.6 (1.55)	104.0–114.0
Loss in splitting (mg)	1752	1.16 (1.78)	0–21.0
Loss in splitting (%)	1752	1.06 (1.63)	0–19.4
Tablet portion weight (mg)	1752	53.7 (7.26)	25.0–80.0
Variation of tablet portion from ideal*	1752	10.2 (8.7)	0–54.9

*Ideal weight 54.3 mg.

re conducted with χ^2 tests for categoric data d F test of analysis of variance for numerical ta. Calculations of descriptive statistics and all atistical tests were conducted using SAS ftware (version 6.11).

esults

Ninety-four volunteers (55 women, 39 men) articipated. A broad distribution of ages was epresented: 34 volunteers were less than 35 ears of age, 36 were age 35–44 years, and 24 were older than 55 years. All had completed high school and 83% had attended college. Most (8[illegible] 1%) were right-handed and one was a dextrous. Sixty-two percent of volunteers h[illegible]ong fingernails. Men had larger hands, on average, than women, as well as correspondingly stronger pinch and grip strengths. Slightly more than one-third of volunteers (35.1%) had experience splitting tablets.

A total of 876 tablets were manually split into 1752 portions and 51 were split into 102 portions with a commercial splitter (Table 2). The mean variation from ideal weight of manually split tablet portions was 10.9%, with approximately 1.1% of a tablet's weight being lost in splitting.

Slightly more than one-third of split tablet portions were within 5% of ideal weight; however, 41.3% deviated from ideal weight by more than 10%, 23.5% by more than 15%, and 12.4% by more than 20% (Figure 2). Similar results were found with the tablet splitter: 40.2% of portions were within 5% of ideal weight, and 37.3% deviated from ideal weight by more than 10%.

Analysis of variance (ANOVA) of the effect of gender, age, education, tablet-splitting experience, and presence of long fingernails failed to identify particular factor that predicted difficulty splitting tablets accurately. Firm grip strength in men was, however, inversely associated with the ability to split tablets accurately (p=0.0001). This factor was not identified as significant for women (p=0.1569). When failure to split a tablet within 15% or 20% of ideal weight was considered as an outcome, none of the demographic factors predicted failure; however, firm grip strength in men was identified by ANOVA to be significantly associated with increased failure at both the 15% and 20% levels. When drug lost in tablet splitting was measured, no patterns were identified that predicted increased loss, except that younger and older volunteers were slightly more likely to cause loss than middle-age volunteers (younger volunteers 1.22 mg lost, middle-age 0.86 mg lost, older 1.17 mg lost; p=0.0082, ANOVA).

Given the choice, 96.8% of volunteers stated that they would rather not split a tablet if a lower-dose formulation was available. Over three-fourths (77.2%) stated that they would be willing to pay more for a lower dosage strength, with the median amount being 20% over the original price of the prescription.

Discussion

Extensive analysis of the ability to split a 25-mg hydrochlorothiazide tablet accurately by 94 volunteers found that the average tablet portion

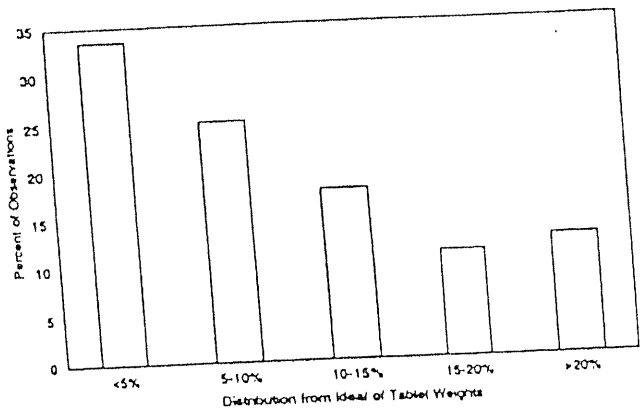

Figure 2. Distribution from ideal of manually split tablet portions.

varied from ideal weight by slightly greater than 10%, and that approximately 1.1% of the weight was lost in the splitting process. In addition, over 40% of portions deviated from ideal weight by greater than 10%, with almost 25% deviating by greater than 15% and over 12% by more than 20%. The use of a tablet splitter did not improve the accuracy of splitting.

Demographic and volunteer-specific data were captured to determine whether certain factors were predictive of inaccurate tablet splitting. Gender, age, education, and tablet-splitting experience were consistently found not to be predictive of accuracy. Only firm grip strength in men was a significant factor in predicting variation of tablet portion weight from ideal; grip strength was not predictive in women. No subpopulation existed that was consistently able to split tablets accurately. Thus, stereotypes regarding which patients might be "expected" to be able to perform this seemingly simple task should be discarded.

In rare circumstances (1.2%), the two tablet portions weighed more than the original whole tablet. This can best be explained by the transfer of finger oils from the subject to the tablet during splitting, and as a result, deviations from ideal may underestimate the true deviation from ideal. Such bias could be avoided with the use of unlubricated latex gloves, but that could have interfered with subjects' ability to split tablets accurately.

Several tablets were evaluated with respect to the percentage variation from ideal when split manually.[1] More than 87% of portions of oval 10-mm tablets with deep scores on both sides were within 10% of ideal weight. In contrast, smaller round tablets were more likely to yield inaccurate segment weights. Only 45% of round 8- or 9-mm tablet portions were within 10% of ideal weight, and 44% of round 7-mm tablet portions deviated from ideal by more than 20%.

The accuracy of a tablet-splitting device was assessed on 13 different agents available in tablet form.[2] The tablets differed in size, shape, and coating. Twenty tablets of each drug were split and the number of 40 resulting portions that were within 15% of ideal weight was determined. The best results were seen with larger tablets (> 600 mg) that were coated, and had an oblong (but not pointed) shape and flat edges. The smallest tablet tested was phenobarbital (+.1 mm, 30 mg), and this was among those with the highest percentage error.

Certain difficulties were observed with the tablet splitter, primarily with placing tablets in the correct position. Hazards associated with the device included potential injury due to the sharp steel blade attached to the lid, and the possibility of combining the present drug with powder or fragments of previously split ones.

As cost containment has become increasingly important, it is apparent that many physicians are responding by prescribing larger dosages of drugs and then instructing patients to split the tablets to receive the correct dose.[15] Some health maintenance organizations are providing tablet splitters to patients while dispensing larger than prescribed tablet sizes. Although this may be less expensive in the short run, it has not been proved to be financially or medically effective. Patients may be reluctant to split the tablets and decide to take double the dose at twice the dosing interval, thus leading to wide swings in blood concentrations. Alternatively, with polypharmacy common in many older patients, instructions regarding which drug to split may not be remembered between the time a prescription is received and the time the agent is taken, thus exposing the patient to unnecessary toxicity.

These results are applicable to other areas of therapy besides antihypertensives. In pediatrics, it is frequently necessary to split tablets, often into thirds or fourths. Although this was not the focus of the present study, it is reasonable to postulate that even greater errors would occur under these conditions. Because of the need to dose many drugs in children on a milligram per kilogram basis, these errors may be more important than in adults.

Our results may underestimate the variation from ideal in tablet portions. Tablets split by a patient in advance and returned to the pill bottle may be additionally subject to increased friability and fragmentation, hygroscopic absorption o water, and altered shelf life due to a break in th tablet's protective coating.

The *United States Pharmacopeia* specifies that dosage formulation should be within ± 10% of i stated value. For most drugs, a variation of mo than 10% probably would not influence ther peutic outcomes. Errors could be of concern f those with narrow therapeutic indexes (e.g digoxin, warfarin), capacity-limited metaboli (e.g., phenytoin), or steep dose-response cur (e.g., hydrochlorothiazide).

Possible future areas of study could b comparative bioequivalence trial of manu split tablets versus a commercially availa formulation to determine if the accep

...nes for establishing bioequivalence are

eferences

1. Gupta P, Gupta K. Broken tablets: does the sum of the parts equal the whole? Am J Hosp Pharm 1988;45:1498.
2. Sedrati M, Arnaud P, Fontan J, Brion F. Splitting tablets in half. Am J Hosp Pharm 1994;51:548–50.
3. Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-V). Arch Intern Med 1993;153: 154–83.
4. Beermann B, Groschinsky-Grind M. Antihypertensive effect of various doses of hydrochlorothiazide and its relation to the plasma level of the drug. Eur J Clin Pharmacol 1978;13: 195–201.
5. McKenney J, Goodman R, Wright J, Rifai N, Aycock D, King M. The effect of low-dose hydrochlorothiazide on blood pressure, serum potassium, and lipoproteins. Pharmacotherapy 1986;6:179–84.
6. Hart W. Lisinopril-hydrochlorothiazide combination compared with the monocomponents in elderly hypertensive patients. J Hum Hypertens 1991;5:85–9.
7. Lang H. The results of a large multicentre study comparing low-dose lisinopril-hydrochlorothiazide with the monocomponents. J Hum Hypertens 1991;5:73–6.
8. Chrysant S. Antihypertensive effectiveness of low-dose lisinopril-hydrochlorothiazide combination. Arch Intern Med 1994;154:737–43.
9. Reaven G, Clinkingbeard C, Jeppesen J, et al. Comparison of the hemodynamic and metabolic effects of low-dose hydrochlorothiazide and lisinopril treatment in obese patients with high blood pressure. Am J Hypertens 1995;8:461–6.
10. Romero R, Castellote E, Ocon J, Wagner B. Controlled multicenter study with quinapril, hydrochlorothiazide, and combination in patients with moderate to severe hypertension. J Cardiovasc Pharmacol 1995;26:114–18.
11. MacKay J, Arcuri K, Goldberg A, Snapinn S, Sweet C. Losartan and low-dose hydrochlorothiazide in patients with essential hypertension. Arch Intern Med 1996;156:278–85.
12. Canter D, Frank G, Knapp L, et al. Quinapril and hydrochlorothiazide combination for control of hypertension: assessment by factorial design. J Hum Hypertens 1994;8: 155–62.
13. Weir M, Weber M, Punzi H, Serfor H, Rosenblatt S, Cady W. A dose escalation trial comparing the combination of diltiazem SR and hydrochlorothiazide with the monotherapies in patients with essential hypertension. J Hum Hypertens 1992;6:133–8.
14. Frishman W, Bryzinski B, Coulson L, et al. A multifactorial trial design to assess combination therapy in hypertension. Arch Intern Med 1994;154:1461–8.
15. Elliott W. The costs of treating hypertension: what are the long-term realities of cost-containment and pharmacoeconomics? Postgrad Med 1996;99:241–8, 251–2.

Medication Diary of Kaiser Patient - Elderly and on Oxyg - three splits at the same time

MONDAY MAY 24, 1999

FLOVENT 3 PUFFS 2X DAY 6:00
COMBIVENT 3 PUFFS 3TIMES DAY
ZESTRIL 1/2 PILL
PRILOSEC 1 PILL
LASIX 1/2 PILL
METHERINE 1 PILL
WELLBUTRIN 1/2 PILL

HHA 7:30-

TIPS
NCPS
VA National Center for Patient Safety

Volume 6, Issue 3 Topics In Patient Safety May/June 2006

Tablet Splitting

By Mariscelle M. Sales, Pharm.D., and Francesca E. Cunningham, Pharm.D.

Background

TABLET SPLITTING is a common practice often recommended by providers and implemented by healthcare systems. Splitting a tablet allows for a lower dose than that manufactured by the pharmaceutical industries, can facilitate administration of large tablets that patients may find difficult to swallow whole, and can give patients access to more expensive medications.

Tablet splitting has many benefits, and consideration of both drug and patient characteristics ensures safe and appropriate use.

Certain physicochemical properties of a drug influence the decision to split. For example, drugs with enteric coatings, extended-release formulations, and some combination products can cause adverse outcomes if split.[1-3]

In one study, elongated tablets scored deeply on both sides broke easily when manually split.[4] Tablet splitting devices were shown to perform best with larger tablets, tablets with flat edges, and oblong tablets without pointed ends.[5]

Drugs with narrow therapeutic windows should only be split if the physicochemical properties are adequate and if the optimal therapeutic response depends on the dose being halved. Also, patients with severe physical or visual impairments may hinder precision in pill splitting.

Tablets come in all shapes and sizes and require sharp instruments to divide them. Patients or their caregivers must have good vision, manual dexterity, and the mental capacity to accurately split a tablet. Accuracy of tablet splitting also depends on one's technique or device.

An optimal tablet-splitting device should have a hard, steel blade that goes all the way into the base when the lid is depressed. This will ensure a clean cut without leaving unusable fragments or crumbs that break off from the tablet. Additional benefits are provided when using a non-slip surface with adjustable grips to firmly hold the tablet steady and an optional magnifying attachment to enlarge the view of small tablets.

Any alteration of a medication may result in an adverse event or close call; hence, tablet splitting may cause problems in the medication use process. Using a good tablet-splitting device, unambiguous directions listed on the prescription, and identification/recognition of non-splittable medications comprise steps that can help to prevent problems from developing.

VA NCPS and the VA Center for Medication Safety Patient Safety Center of Inquiry (PSCI) embarked on an effort to evaluate potential medication problems caused by tablet splitting. Data on tablet-splitting events were evaluated using the NCPS Patient Safety Information System database (nicknamed "SPOT"). This article describes the results of that analysis.

Analyzing SPOT Data

Methods:

NCPS identified tablet splitting entries by querying the SPOT database for all RCA and safety reports involving tablet splitting from January 2001 to April 2005, forwarding the results to our Patient Safety Center of Inquiry for analysis. Search terms included: pill splitting, tablet splitting, half tablet, quarter tablet, ½ tab, and ¼ tab.

Data provided for each event included an anonymized case ID; date (year); free text description of event details; and record type (aggregate, safety report, RCA).

A complete evaluation of reports was conducted. Analysis of each individual case determined:

- Type of event (actual adverse event, close call, not enough information, or "other")
- Location of occurrence (inpatient or outpatient)
- Error type (overdose, underdose, incorrect directions, incorrect quantity, incorrect day supply, and incorrect strength dispensed)
- Medication characteristics (correct physicochemical properties, to include: non-extended release, no enteric coating and symmetric in shape; commercially available strengths; and high alert medications[6])
- Documented patient outcomes (no harm, minor harm, hospitalization, and/or permanent harm/death)

Results:

We found 442 reports in SPOT related to pill splitting. Below are selected, notable statistics from these events:

- 38% were adverse events
- 66% of the adverse events involved patients receiving more than their intended dose
- 65% of the adverse events occurred in outpatient settings
- 51% of the adverse events involved medications that came in commercially available strengths
- 28% of the medications were high alert
- 9% of the adverse events resulted in causing harm to a patient, but only 2% required hospitalization; no deaths were reported

Discussion

Limited literature suggests that manually or mechanically splitting tablets does not always produce equal portions.[7-15] The current evaluation of tablet splitting events within the VA revealed no problems regarding accuracy in splitting tablets to produce equal halves.

However, a potential source for problems was found in a number of areas: ordering, verifying, filling, and administering medications that require splitting.

continued on back page

Subj: **Re: questions about details of pill splting**
Date: 1/28/2007 1:40:51 P.M. Pacific Standard Time
From: daretodream94704@yahoo.com
To: CPhil49401@aol.com

yes and here is my picture
CPhil49401@aol.com wrote:

> So you get to sleepy once a day and no relief once a day because they will not supply you with the 2mg tablet to take twice a day.
>
> In a message dated 1/27/2007 9:27:57 P.M. Pacific Standard Time, daretodream94704@yahoo.com writes:
>
> > The Baclofen did not work , It made me fall asleep .
> > You right about the 4mg . I was supposed to take it twice a day ,and now I take it just once.
> > thanks

Nicholas Feldman
Dare to Dream Attendant Services, LLC
275 5th St. #203
San Francisco, CA 94102
(800)988-9927
Fax: (415)541-8590
website: www.daretodreamattendantservices.com
blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Subj: **Re: questions about details of pill splting**
Date: 1/27/2007 9:27:57 P.M. Pacific Standard Time
From: daretodream94704@yahoo.com
To: cphil49401@aol.com

The Baclofen did not work , It made me fall asleep .
You right about the 4mg . I was supposed to take it twice a day ,and now I take it just once.
thanks

cphil49401@aol.com wrote:

> My pocket book of medications that I carry as an emergency physician states:
>
> "tizanidine (Zanflex): muscle spaticity due to MS or spinal cord injury: 4-8 mg PO q 6-8 pm, max 36 mg/d. [Generic/Trade: Tabs 2 & 4 mg, scored. Trade 6 mg.] $$$$"
>
> I'm thinking you are being asked to split the 4 mg. How often were you supposed to take it? Did you try Baclofen and compare? Dr. Phillips
>
> -----Original Message-----
> From: daretodream94704@yahoo.com
> To: cphil49401@aol.com
> Sent: Sat, 27 Jan 2007 4:21 PM
> Subject: Re: questions about details of pill splting
>
> 2.5 miligrams
>
> ***cphil49401@aol.com*** wrote:
>
> > Now I need the strength of the pill to verify that the half dose size was available as a full size pill either on the Kaiser formulary or to be bought. Dr. Phillips
> >
> > -----Original Message-----
> > From: daretodream94704@yahoo.com
> > To: CPhil49401@aol.com
> > Sent: Sat, 27 Jan 2007 2:04 PM
> > Subject: Re: questions about details of pill splting
> >
> > Dear Dr. Phillips,
> >
> > The answers are below in italics. I really hope this makes a difference, and that the pharmacy board really does something. We need more advocates like you.
> >
> > Thanks,
> > Nick Feldman
> >
> > ***CPhil49401@aol.com*** wrote:
> >
> > > 1. Tell me about your general health and whether you could be expected by dexterity to split pills. *I have cerebal palsy in all of my limbs. Kaiser wanted me to split my Zanaflex to help reduce my spasticity.*

2. Tell me if your physician explained that you would be asked to split pills or whether it happened at the pharmacy window. *The woman at the pharmacy counter very casually told me that I can split the pill to help spread it out longer.*

3. Tell me the name of the pill and how long the splitting lasted. *Zanaflex...indefinately*

4. Tell me if you gave up on splitting and simply take the whole dose every other day. *I gave up because I was not comfortable with my assistants having to split the pills. I also was never given a pill splitter, so determining what half the pill really is is really hard.*

5. Tell me if you have explained this to your physician or the pharmacist. Was any action taken? *Yes. No action was taken.*

6. Did you get any pill safety handout? *No*

7. Do you experience any side effects with the whole pill? *Yes. Drowsiness.*

8. Would you rather have the right does in a smaller pill? *Yes*

9. Can I share your answers with the California Board of Pharmacy and thus the public? *Yes*

10. Where do you live? Where do you get your care from Kaiser? *I live in downtown San Francisco, and I am seen at the Kaiser on Divisadero, and also at the French campus.*

Dr. Phillips

Nicholas Feldman
Dare to Dream Attendant Services, LLC
275 5th St. #203

San Francisco, CA 94102
(800)988-9927
Fax: (415)541-8590
website: www.daretodreamattendantservices.com
blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Nicholas Feldman
Dare to Dream Attendant Services, LLC
275 5th St. #203
San Francisco, CA 94102
(800)988-9927
Fax: (415)541-8590
website: www.daretodreamattendantservices.com
blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Nicholas Feldman
Dare to Dream Attendant Services, LLC
275 5th St. #203
San Francisco, CA 94102
(800)988-9927
Fax: (415)541-8590
website: www.daretodreamattendantservices.com
blog: http://mydreamweaver.blogspot.com/
(Assistant may answer the phone)

Timolol [MC] *(Continued)*

vomiting, stomach discomfort, numbness in toes and fingers, dry sore eyes

Usual Dosage Children and Adults: Ophthalmic: Initial: 0.25% solution, instill 1 drop twice daily; increase to 0.5% solution if response not adequate; decrease to 1 drop/day if controlled; do not exceed 1 drop twice daily of 0.5% solution

Dosage Forms

Solution, as hemihydrate, ophthalmic (Betimol®) [$$$]: 0.25% (5 mL, 10 mL, 15 mL); 0.5% (5 mL, 10 mL, 15 mL)

Solution, as maleate ophthalmic (generic Timoptic®) [$$]: 0.25% (5 mL, 10 mL, 15 mL); 0.5% (5 mL, 10 mL, 15 mL)

Solution, as maleate, ophthalmic, preservative free, single use (Timoptic® OcuDose®) [$$$$$]: 0.25%, 0.5%

Recommended Alternative Levobunolol is the preferred ophthalmic beta-blocker

Generic Available No

- **Timoptic®** *see* Timolol [MC] *on page 743*
- **Tioguanine** *see* Thioguanine [MC] *on page 735*

Tiopronin

Brand Names Thiola™

Therapeutic Class 60:15 Resins & Chelating Agents

Use Prevention of kidney stone (cystine) formation in patients with severe homozygous cystinuria who have urinary cystine >500 mg/day who are resistant to treatment with high fluid intake, alkali, and diet modification, or who have had adverse reactions to penicillamine

Usual Dosage Adults: Initial dose is 800 mg/day, average dose is 1000 mg/day

Dosage Forms Tablet, 100 mg

Generic Available No

- **Tiotixene** *see* Thiothixene [MC] $$ *on page 739*
- **Tissue Plasminogen Activator, Recombinant** *see* Alteplase, Recombinant *on page 106*

Tizanidine $$$$$

Brand Names Zanaflex®

Synonyms Sirdalud™

Therapeutic Class 30:40.15 Skeletal Muscle Relaxants, Centrally-Acting Agents

Use Skeletal muscle relaxant used for the acute and intermittent management of increased muscle tone associated with spasticity

Contraindications Previous hypersensitivity to tizanidine

Warnings Reduce dose in patients with liver or renal disease; use with caution in patients with hypotension or cardiac disease. Use with caution in patients receiving antihypertensives. Do not use tizanidine in patients receiving alpha$_2$-adrenergic agonists.

Adverse Reactions

>10%: Hypotension, sedation, daytime drowsiness, somnolence, xerostomia

1% to 10%: Bradycardia, syncope, fatigue, dizziness, anxiety, nervousness, insomnia, pruritus, skin rash, nausea, vomiting, dyspepsia, constipation, diarrhea, elevation of liver enzymes, muscle weakness, tremor

<1%: Palpitations, ventricular extrasystoles, psychotic-like symptoms, visual hallucinations, delusions, hepatic failure

Kaiser

Drug Interactions

Oral contraceptives decrease tizanidine clearance.

Increased toxicity: Additive hypotensive effects may be seen with diuretics, other alpha adrenergic agonists, or antihypertensives; CNS depression with alcohol, baclofen or other CNS depressants

Usual Dosage

Adults: 2-4 mg 3 times/day

Usual initial dose: 4 mg, may increase by 2-4 mg as needed for satisfactory reduction of muscle tone every 6-8 hours to a maximum of three doses in any 24 hour period

Maximum dose: 36 mg/day

Renal/hepatic impairment: Reduce dosage

Monitoring Parameters Monitor liver function (aminotransferases) at baseline, 1, 3, 6 months and then periodically thereafter

Additional Information Tizanidine is a centrally-acting alpha$_2$-adrenergic agonist with dose-dependent effects and is pharmacologically similar to clonidine. Patients should be counseled regarding the possibility of hypotension after the first dose. During trials the reduction in blood pressure was seen within 1 hour after dosing, and peaked at 2-3 hours after the dose. At times the hypotension was associated with bradycardia, orthostatic hypotension, lightheadedness, dizziness, and syncope (rare). Clinical trial data suggests that tizanidine is not associated with muscle weakness like baclofen. However, this finding also did not lead to any consistent advantage as measured by activities of daily living. Data on the long-term administration of tizanidine are limited. No rebound hypertension was seen during clinical trials when tizanidine was tapered over 7 days.

Dosage Forms Tablet: 4 mg

Generic Available No

- **TNKase™** *see* Tenecteplase [FG] $$$$$ *on page 725*
- **TOBI™ Inhalation Solution [FR]** *see* Tobramycin [FR] [MC] *on page 745*

Tobramycin [FR] [MC]

Brand Names Nebcin® Injection; TOBI™ Inhalation Solution [FR]; Tobrex® Ophthalmic

Therapeutic Class 05:05.05 Aminoglycosides; 75:25.05 Anti-Infectives, Ophthalmic

Use Treatment of documented or suspected *Pseudomonas aeruginosa* infection; infection with a nonpseudomonal enteric bacillus which is more sensitive to tobramycin than gentamicin based on susceptibility tests; susceptible organisms in lower respiratory tract infections, CNS infections, intra-abdominal, skin, bone, and urinary tract infections; empiric therapy in cystic fibrosis and immunocompromised patients; topically used to treat superficial ophthalmic infections caused by susceptible bacteria

Restrictions *Formulary*: Tobramycin solution for inhalation (TOBI™) is restricted to prescribing CF Subspecialists, Pediatric and Adult Pulmonology

Pregnancy Risk Factor D

(Continued)

AT Journal
The Latest News & Resources in Assistive Technology
Vol. 97, May 15, 2004

A Personal Perspective...

By Nicholas W. Feldman

I can remember being 5 years old and my family all clustered around me, watching as I played my first video game using a chin control as I shot at the spaceships on the screen. It was 1980 and the Apple 2 + was all the rage. I had no idea what a significant role technology would play in my life as I grew up with Cerebral Palsy (CP).

Like a lot of children with CP, I went from school to school trying to find that, "equal education" that creates the integrated environment and allows the student with the disability to soar to their full potential. I sat in a special education kindergarten class where they told me about single input scanning. This is where you press a switch, using any part of the body (within reason) and it is connected to the CPU by a box. This then displays a row of letters, numbers, punctuation and a few very select groups of menu commands. The highlighted areas were divided into sections and if you pressed the switch in the right section, it would break down the individual letters, numbers and other symbols and when it would finally land on the right key, you would press the switch again and it would type it on the screen.

I am very verbal and my friend sitting next to me in that special education class was non-verbal and a lot was assumed for her. She was constantly told what to eat, what to wear, what to do and where she would go, via the request of our teacher to the classroom assistant. Then, one fine day, the teacher came to me and asked if I would empower my friend who was learning to do single input scanning, not on a computer per say, but a large board with different color lights with signs that said words like yes, no, bathroom, I want to eat, etc. My friend was very shy until that special board came along. The school had no idea what they were in for. Suddenly, questions that were once assumed now had different color lights and a whole personality to follow. I soon moved away and never really knew, but had a good imagination about my shy friend who, at age 6, finally got the opportunity to start making her own choices.

As I moved to different schools, with different levels of academic demand, I was still struggling with my single input scanning. I used a switch that was connected to a pillow on my headrest. I was doing this, but I had my sites set on bigger things like

being mobile with a power wheelchair. The technology had to allow me the ability to use my head to control a wheelchair. There was a company in Ohio, which had technology very similar to what I was using to activate the computer. The wheelchair worked with a switch that was fastened to my headrest and when it was pushed, lights would flash on different arrows labeled "forward", "right", "left", "back" and all of the diagonal directions. To stop, the switch would need to be pushed again. By this time frame, it was the late 1980's and very early '90s. I was beginning to hear about not only portable computers, but I was fantasizing about sending an email to a friend in my car pool. Slowly, the Internet began to evolve and our family got its first subscription to an online service called Prodigy. I remember the first email I sent, was to my cousin who was serving in the military during the first invasion of Iraq.

Simultaneously, I was entering high school and was given a laptop computer and a new single input scanning system called words plus. This system had a feature called word prediction, which allows a slow type such as myself to have a list of possible words to choose from as you are typing. This vocabulary is primarily built by the words that it will remember after you type the word along with its own 68,000-word vocabulary. This made all the difference in the world especially when it came to book reports, essays, poetry, and letters that you weren't going to let your folks read.

The Internet was still in the first phase of the "web" and I was going into my junior year of high school. Someone with CP came down and demonstrated a voice activated program known as DragonDictate. This program, I had an opportunity to try out through a local computer access center which I was then affiliated with on an after school/volunteer basis. I became aware of some of the power in the Internet and through assistive technology such as the head master which has an infrared connection with a band that the user places around their forehead which emulates the mouse and a straw that the user uses to click and drag the mouse. There were now keyboards that would speak and new advancements in technology, which seemed to happen every millisecond.

I was just about to graduate from high school when I got a new type of wheelchair that had 3 switches that meant that with a new feature called "Cruise Control"; I could drive my wheelchair easier by pressing switches located on the sides of my headrest and one accelerator/brake. These features allowed me to drive and turn at the same time.

UC Berkeley was waiting for me with a big dose of Independent Living and much more of the Internet and disability culture. As I sit here speaking into my DragonDictate Classic controller along with a wheelchair, which I operate with my chin, I can function a lot more independently. I have worked with a lot of different access centers and independent living centers as well as the Department of Rehabilitation in order to fund all of this technology, which I had never dreamed of. I

even have a door opener that I can use with my headrest and a voice activated cell phone.

As an individual, my cerebral palsy has created some societal barriers, which the Internet breaks down. With a video camera and a microphone, everyone who I am in contact with is not always aware that I have a disability. Through all of my years, assistive technology has played an intricate role in so many areas of my life that includes: social (I, after 26 years, have a girlfriend, thank you messenger service), educational (typed and edited many college papers), housing (search through housing websites), and employment where I have had past jobs (dispatcher, independent living skills program coordinator, interim executive director of a non profit) and I currently work as the Oakland Center for Independent living as a Systems Change Advocate. As I go into the post education and job world, I continue to rely on assistive technology to help be my office for whatever opportunities await me. There is also the expectation that technology will continue to allow me the advancement and growth to continue affording me the opportunities that life with and without a disability has to offer and enjoy. I am hoping that the day will arrive when I say "get me up", a robot will be able to make my breakfast, program driving directions into my van, read me the latest email and news, walk my dog and vacuum the floor.

[AT JOURNAL | JOURNAL INDEX]

(Charles Phillips, MD, FACEP, 2216 E. Los Altos Ave.Fresno, CA 93710

Cphil49401@aol.com Cell – 559-917-8997 (after 10 AM)

PRESENTATION ON 4/3/07 TO

THE CALIFORNIA BOARD OF PHARMACH

ON PILL FRAGMENTATION -

REBUTTAL OF SAN DIEGO PUBLIC TESTIMONY –

Subcommittee on Communication and Public Education Meetings

Once again, thank you for letting me come to the microphone, this time for the focus of what might be the correct patient information that should be published about pill splitting (never to allowed to be called Pill Halving or Half Pill Program because of the rarity of a half and the high likelihood of very uneven fragments). This right for clear information to bring the patient to the level of the provider as much as possible and to empower the patient to have real choices is the principle of "autonomy." Paternalistic medicine by those with white coats is gone forever (except in Singapore) and that patients must actually make their own decision. That is where we get INFORMED consent. It is echoed on the wall of every accredited hospital[9], in the Board of Pharmacy "Patient's Bill of Rights"[10] (Exhibit #5), and the VA's "Patient and Nursing Home Resident Rights and Responsibilities[11].

[9] In Kaiser Fresno this paper is behind a patient waiting chair in x-ray such that other patients would be highly unlikely to read it. Two miles away at Saint Agnes Hospital the same paper is next to the public's coffee machine in the registration area where most patients and/or families will see it. The Joint Commission has as their first chapter in accreditation Patient Rights.

[10] I would like to see these rights print out easily in portrait rather than landscape form so patients can actually read them easily as they come to a pharmacy window and have their high trust interaction.

[11] Hippocrates did not seem to have to trade the gift of a professional oath (this world) and covenant (the next world) for patients having to perform in any way; now it is phrased as some even trade between business associates. Patients do not join practices, practitioners join families.

I will try to improve on the two best examples of patient education on pill splitting that I could find on many hours of computer research: the VA's approach in Indiana VA and the Benefits Office of the University of Michigan. Using those two fine examples of trying to get it right – both specifying the sequential use of split fragments – I have tried to create my own consent requirements:

1. Your prescription has the option of being filled by pills that are split into usually unequal pieces for the saving of health system moneys; you have a right to know where this money goes since you are taking on the disease risk of uneven dosing;[12]

2. after reading all of these notes you can chose to have the split of the double size pill approach or the unsplit whole pill without any pressure, influence, criticism, fear of reprisal, or thought that your caregiver might even be annoyed (in case he or she is tracked for pharmacy costs of his or her patients);

3. The research on this topic involved patients who split their pills every day and took the large and small fragments within two days, thus balancing out the dosage; these were on pills that stick around a long time so it has been presumed safe.

4. If you are being asked to split pills in large numbers all at once, there is no research to say that is safe and, in fact, it would be most likely unsafe[13]; bouncing cholesterol, blood pressure, diabetes, etc. has no likelihood of being safe and is most likely to accelerate your disease process;

5. The most common problem surfacing in pill splitting - as discovered by NASA in the contract review of VA practices – is the doubling of pills, and this commonly occurs to about 9% of the splitters about three times a month; your physician and pharmacist need to be sure that a double dose is safe for you on occasion (too tired to split a pill some sleepy morning);

6. There is also no science that says that if you split 200 days of medication that the exposed surfaces of the pills will not add oxygen or water in a way that changes their effect, since pill splitting was never part of the animal or human studies on the way to this after sale practice of dispensing; there have been warnings about this;

---

[12] This would be the place where an HMO could explain the vast savings that accrue and the split of profits with the physicians. Perhaps the accumulation of $1 billion by CEO Dr. William Mc Guire while making these decisions might suggest that his decisions involved a hand in the cookie jar. I once tried to talk him out of pill splitting; but he continued undaunted.

[13] Note Kaiser has offered up no research of its own, although a surprising number of investigators on this topic have ended up Kaiser-financed-related before the day of publication – two pharmacists and one "pharmaco-economist." It is unclear to me whether or not Dr. Stafford, the pharmaco-economist - who did not study safety in pill splitting beyond the theoretical – ever gave out one pill in his life. His supposed ties to Harvard, Yale, and Stanford did not seem to change the practice – almost no pill splitting – of any of them.

7. The newest pill splitters – which you need to request – have child safety plastics that prevent fingers from being cut; but no splitter is child proof to be opened so that any pills or fragments left in the pill splitter can be of harm to your children, grandchildren, or young visitors;

8. You need to replace the one or several pill fragments back into your pill bottle but be able to find them before they migrate down to the bottom; ask your pharmacist how to do this safely;

9. The average time calculated in the US and Canada for safe counseling on pill splitters by pharmacy students or pharmacists is considerable[14]; expect that counseling to be needed on the first few refills and twice a year so that you do not fall into several common error patterns;

10. The California Board of Pharmacy would like to hear about any errors that occur in pill splitting as this largest of states at phone number 916-___-____.

Please sign that you have read this safety sheet - _____.

END OF SECOND PRESENTATION - CP

[14] Canada decided that the time needed to do this safely ate up any profit expected.

Charles Phillips, MD, FACEP, Fresno, CA

Cphil49401@aol.com

Cell – 559-917-8997 (after 10 AM)

PRESENTATION ON 4/3/07 TO THE CALIFORNIA BOARD OF PHARMACY ON PILL FRAGMENTATION - REBUTTAL OF SAN DIEGO PUBLIC TESTIMONY – Subcommittee on Legislation and Regulation

Members of the Pharmacy Board, the Board staff, the audience, and the public served by this consumer protection activity, thank you for letting me come to the microphone again on the topic of the safety of pill handling between pharmacist and the moment of patient swallowing. This is my third appearance which represents your appropriate focus on what is a major source of abuse to seniors and the disabled, if not all patients participating. I do not mind the driving effort from Fresno; I have spent more time on this topic than any other physician in the country (when the AMA is asked about this topic, they refer the reporters to me).

Pill splitting – more accurately **pill fragmenting** – appears today on **two** Pharmacy Board subcommittees. This is appropriate because there is a need to first review real **patient safety**[1]

---

1 Last Friday I received an Email alert from Maggie Dee – San Francisco radio show host – that "20-20" was going to have a long segment that night on frontline pharmacy safety. I thought the show was accurate as well as scary. While states were not mentioned, I have personally witnessed many of the allegations in California. I particularly noticed that the problem was often related to the pharmacy business managers just above the frontline professionals - in which the pharmacy tasks cannot be done safely simply by pure volume of prescriptions to be filled. There appears to be a dark-hole vacuum of responsibility above the frontline, so that the manipulators of pharmacy "benefits" and the bosses of the frontline providers keep the license boards aimed at the moments of error rather than the systems that made it inevitable. **As long as we search only for rotten apples, we will miss the obvious rotten barrels that populate this universe of care.**

The pharmacist – like the physician – in managed care is turned into a "profit center" and the patients are only "external customers." The professional who get ahead are those who put all the risk on the patient by delegating the care to those least trained and thus least expensive. This is the same ethic as that is pictured by one pharmacy chain outlet Kaiser (on the internally developed Permanente Medicine Map) as the "group ethic" which is the "wind" of the Permanente Fleet. The goal is to replace the frontline Hippocratic Oath relationship with the ethic-challenge approach called the "Permanente-Patient relationship." Frontline providers are only hourly-paid cassette tapes moved around as spaces open up. Unfortunately, the Board will be

and then to see if this delivery strategy – if still standing in some form after such an evaluation – can be communicated through educational means in some way respectful to **a patient's rights to know the risk and benefit of any medical treatment.** The Western patient has – since the Nuremberg Trials showed how easily physicians can stray from care to harm – appropriately demanded and obtained the principle of "autonomy" to actually make decisions once fully and honestly informed.

For this Legislation/Regulation Committee then, I will focus on the lack of safety with pill splitting – keeping my comments brief, without repetition of early material, and responding mostly in rebuttal. I will also include summarizing some recent email interactions I have had with VA research personnel, patients who are splitting in various states and clinical settings, and Dr. Mark Aramowicz, the three decade Editor of The Medical Letter.

As Kaiser has deposed me on this topic with some two days of video-taped interview under penalty of perjury and thereafter to risk to my license if speaking any untruth, I would like to state that the comments I make here today will be given as if under oath - so that the Board is not lead astray. **I would ask that the others speaking on this topic also hold themselves to the same oath and license standard.** We are practicing medicine and pharmacy whether we are at the front doors of care or in far away cities stating in testimony to what is safe and unsafe. The AMA, in fact, would like to see all those in managed care be viewed as practicing medicine, particularly when care is rationed, modified off standard, or otherwise curtailed.[2]

First of all, pill splitting was depicted by Mr. Steven Gray of Kaiser[3] at your last meeting as safe. The pictorial held up was that of the Consumer Reports magazine which does, in fact, say "Pill-Splitting – It's safe and can save you lots of money." [See exhibit #1]. So I E-mailed the Consumer Union and found that they had leaned heavy for their anonymous article on another non-profit foundation that they claim to have initiated – The Medical Letter. After much search I found the anonymous 2004 article (Exhibit #2). And after further search I reached the Editor for the last 30 years – Dr. Arbramowicz of New York. We exchanged some E-mail. I told him that the article was fair in the sense that it described accurately the great difference in split pill sizes – **51% falling outside the USP limits on generics of 85% to 115% and that physicians and pharmacists were to make sure pills were split one at a time so that the low dose would**

---

encouraged to have pharmacy students with new and fragile ethics spend more time with the manipulators of the game rather than those struggling in offices, emergency rooms, and pharmacies to do the job the way they were trained and within the White Coat mantel.

[2] When I had a private office, I would often find myself fighting for a patient to get the correct medicine and after listening to country music getting a pharmacy tech in Iowa who would read me the rules of some HMO. I always won the issue, but lost the time and finally closed my office.

[3] Background unknown to me so far.

match the next day's high dose. (The Consumer Reports said the same – far into the article).

He said The Medical Letter will be drafting another article on pill splitting after my interactions this last month, this time – I believe after studying the 422 errors in the VA over 3 years – he will probably be even more insistent that **should there be a pill split, the first day's fragment must be followed the second day by the other fragment. And with the high rate of pill doubling going on, there must be much more attention to slow implementation to person by person with a lot of education and close follow up.**

I think that when the Hippocratic Oath is reapplied to this practice, the time needed to do this right will – as well explained in the Canadian article in your attachments by staff – be so excessive in teaching that all economic gains are lost. It will be even more clear than it is now, that the Kaiser approach of giving patients 100 pills to be split into 200 uneven pieces with no careful instruction, no safety paper[4] does not match either the Consumer Report (or the Medical Letter article) though advanced before this Board as a form of validation for what this for profit HMO does.

As to the idea that pill splitting is "voluntary," that totally ignores both the fact that the patient is given no information about risks and benefits and the enormous unwillingness of patients to question professionals in the absence of such information. I have never had a patient agree to splitting after hearing the real risks and benefits of bouncing medication. None of the Kaiser patients in Timmis v. Kaiser (Exhibit #3) thought that they had any choice.[5] And in the case of Nicholas I mentioned in Sacramento testimony, he was expressly lied to that Kaiser did not have his pill in the two milligram size; it is present in every Kaiser hospital formulary since nurses would refuse this silliness.

I do agree with Mr. Gray that the practice is endorsed by the Permanente committees (aka the Permanente Federation members that dominate the P+T Committee where pharmacists do not even vote). But that has more to do with their split of profits and plush retirements than with any science that could stand the light of day. And the Pharmacy Board does have the consumer protection role to judge if this is safe, physician partnership for profit ruling or not. Actually, Kaiser is not even following the guidance of the Academy of Managed Care Pharmacy on this issue – they have published that pills must be split one at a time.

---

[4] The Kaiser explanation paper presented as handed ot to all patients – advanced during the court battle on splitting called Timmis v. Kaiser as part of the safety system – can no longer be located if a patient or physician so requests (as I did again yesterday in a Kaiser pharmacy). I have verified this at several locations. There are simply splitters and pills. And the average training of those assisting the pharmacist needs to be rechecked; the 20-20 suggestion of students in training in frontline pharmacies is highly accurate for many.

[5] Audrey Timmis had no choice because Kaiser only ordered the high dosed Mazide for outpatient use; the normal dose for seniors reserved for hospital use only.

Dr. Anthony Morielli – who next spoke to you - was a bit humble about his many titles as he spoke for the benefits managers point of view in the VA. He is the West Coast head of benefits as well as the chief pharmacy of the VA in San Diego. The idea that he simply "works for the VA" in your minutes is an understatement. Of course, he cannot represent the VA in calling the practice safe because **the VA has not endorsed it after all their "research."** Their Technical Advisory Committee in Massachusetts will not let them! Dr. Morielli started pill splitting, research following practice, though wondering by Email to me who told me (no denial mentioned)[6]; he bears great responsibility if it unsafe.

I have been in communication with a VA pill splitting researcher (Exhibit #4) who said very clearly that the VA in the largest splitting area – Tampa – has made sure that pills are split one at a time due to unequal weight. I asked him why this was not explained very often in their research; HMOs never using this safety step. He was not sure and new that it was explained in oral presentations. Research that does not clarify methodology is not valid research.

A careful reading of the VA articles show that the vets are compliant, that the pills are very unequal in size, that pill doubling is a big problem, and that there has to be a matching of fragment sizes.

This leads me to my poster review of the problem as I head toward my conclusion:

1. (Poster One) Pill splitting is inherently unequal, going beyond the safe limits whether or not there is a split line; the only even split is that envisioned in a new product (Poster Two);

2. (Poster Three) HMOs who have taken the VA research and dropped out the safety steps need to be held responsible – I pity the frontline pharmacists and wish the Board to look more closely at the high-rises of power;

3. (Poster Four) The loose science involved creates a house of cards[7] in which there is really no proof of any safety and clear likelihood of danger in the methods used in HMOs to give medications to seniors; these are often blood pressure pills, diabetic pills[8], etc.

4. (Poster Five) The judges in Timmis v. Kaiser have handed the responsibility back to the Boards; it is up to you to represent the people;

---

[6] "How did you know that pill splitting was first tried successfully be me at the VA San Diego?" – 1/31/07

[7] This is a term I am borrowing from a book by about the same title describing the HMOs in Guam, where I set up the paramedic system.

[8] Tolazamide (Tolinase) has been one of Kaiser's favorite splits – read in the PDR about the warnings to seniors for hypoglycemia at night. Stanford considers this a museum pill.

5. (Poster Six) This will be my summary – watch as we go from Brand, to generic, to VA research split with common doubling, to HMO split with steady decrease of pill dosage and or bouncing effect.

Conclusion

This is patient abuse. It is most dangerous for seniors or those with disabilities. I recognized it in 1998. With one surprise visit, any of you could see for your own eyes what is in those pill bottles called medication.

Pill splitting was invented for financial and not clinical reasons. The managers have ignored the safety precautions. Many have already been harmed in the silent processes of hypertension, diabetes, arteriosclerosis, etc. What looked like a way to save money will cost patients billions of dollars.

There are probably 1 million pills a day split in California alone. Any delay in Board decision will cost those involved the predictable harm of uneven dosing. I ask you to act – for Audrey Timmis, Mary O'Donnell, Maggie Dee, Nicholas Feldman, and many others.

END OF FIRST PRESENTATION – CP

The Medical Letter®

On Drugs and Therapeutics

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, NY 10801 • A Nonprofit Publication

www.medicalletter.org

Volume 46 (Issue 1195)
November 8, 2004

IN THIS ISSUE

Tablet Splitting

Breaking drug tablets in half is a common practice. In some cases, a lower drug dose may be as effective as a higher one, with fewer adverse effects. Sometimes tablets are split to achieve an intermediate dose between marketed strengths. When 2 tablet sizes cost the same, as they often do, splitting the larger size saves money. Is this a reasonable practice?

DOSAGE UNIFORMITY — The distribution of active drug in a whole tablet, or its potential for crumbling or breaking unevenly, is related to drug manufacturing quality assurance standards. In one study, using near-infrared spectroscopic imaging, large clumps of active ingredient were found in simvastatin tablets manufactured in 4 countries by secondary manufacturers, but not in tablets manufactured by Merck in the US.[1]

STUDIES — In 3 studies that included more than 22 US-manufactured scored and unscored tablets that were split by pharmacy technicians, split tablets were considered to contain half the dose if they weighed 85-115% of half the mean weight of the whole tablet. Homogeneous distribution of the drug throughout the tablet was assumed. Weight uniformity requirements were met by 7 (32%) of 22,[2] 3 (27%) of 11,[3] and 8 (67%) of 12 drugs tested.[4] Even some scored tablets did not split evenly.

In another study, a licensed pharmacist and two Pharm.D. students split unscored generic cyclobenzaprine 10-mg tablets. The study was sponsored by the manufacturer of the brand name equivalent, *Flexeril*, which is available as a 5-mg tablet (the generic is not). After splitting the tablets with a pill cutter, the weights of the tablet halves ranged from 69% to 130% of the expected weight, corresponding to an estimated drug content of 3.5-6.5 mg per half tablet, assuming uniform distribution of active ingredient within the tablet. Use of a kitchen knife resulted in tablet halves weighing 50-150% of the expected weight, with an estimated drug content of 2.5-7.5 mg per half tablet.[5]

A study assessing the ability of elderly patients to split warfarin (*Coumadin*, and others), simvastatin *(Zocor)*, metoprolol (*Lopressor*, and others) and lisinopril (*Zestril*, *Prinivil*, and others) found that the weights of the half tablets deviated by 9-37% from the expected weight.[6]

CLINICAL OUTCOMES — Two clinical studies enrolling a total of 2,128 patients taking statins described the effects of tablet-splitting programs conducted by two VA health care systems. No undesirable changes in cholesterol levels were detected in patients who took half tablets for six weeks or more.[7,8]

In a crossover study, 29 patients taking a stable dose of lisinopril for hypertension were randomized to receive either a whole or split tablet once daily for two weeks; no statistically significant differences in systolic or diastolic blood pressure were found between treatment groups.[9]

COST EFFECTIVENESS — Tablet splitting can reduce prescription costs by as much as 50% because many drugs cost the same regardless of tablet strength.[10] In separate studies of two VA health care systems, one reported a savings of $138,108 (39%) over one year from a tablet-splitting program with atorvastatin, lovastatin and simvas-

The quarterly newsletter of The TLPJ Foundation

PUBLIC JUSTICE

Winter 2001

TLPJ Files Class Action against Kaiser Permanente for Forcing HMO Members to Split Pills

Mandatory Pill-Splitting Policy Values Profits Over Patients' Health

Trial Lawyers for Public Justice filed a class action lawsuit on December 6, charging that the country's largest HMO, Kaiser Permanente, is violating California law by forcing its members to split prescription pills. The suit contends that Kaiser's mandatory pill-splitting policy endangers patients' health solely to enhance the HMO's profits. It seeks a court order barring Kaiser from forcing its members to split pills and requiring the HMO to disgorge all profits made from this dangerous policy.

"Kaiser's mandatory pill-splitting policy is an outrageous example of an HMO valuing its profits over its members' health and safety," said TLPJ lead co-counsel Sharon J. Arkin of Robinson, Calcagnie & Robinson in Newport Beach, California. "It makes Kaiser millions, but it has no possible therapeutic value and it puts patients' health at risk."

Kaiser adopted its pill-splitting policy because it allows Kaiser to profit from the fact that smaller dose versions of most prescription pills cost Kaiser almost as much as larger dose versions of the same pills. So, Kaiser forces patients prescribed the smaller dose pills to accept and split the larger dose pills – and pockets the enormous cost difference. For example, 50-milligram tablets of Zoloft, a commonly used antidepressant, cost approximately $227 per 100 pills, so it would ordinarily cost Kaiser $454 to provide a patient prescribed 50 milligrams per day with 200

See Pill-splitting, page 10.

Photo by Xiang Zhou

Plaintiff Audrey Timmis

Inside

Project ACCESS Battles Secrecy in Goodyear Tire Safety Case

Despite Death Toll, Key Documents Remain Secret

Trial Lawyers for Public Justice and Consumers for Auto Reliability and Safety (CARS) are seeking public access to key documents and testimony about the dangers of Goodyear 16-inch Load Range E light truck tires. Press reports have disclosed a growing number of deaths and injuries involving these tires, but the documents and testimony about the tires' dangers remain under seal in a New Jersey case. The case was filed after three U.S. Air Force personnel riding in a General Motors Suburban were killed and three others were injured when a Goodyear tire came apart and their vehicle rolled over.

TLPJ and CARS moved to unseal the documents because of their concern for public safety. The challenge to secrecy in the case was filed as part of Project ACCESS, TLPJ's 12-year-old nationwide campaign against unnecessary secrecy in the courts.

"Court secrecy should not be used to hide potential dangers from the public," said TLPJ Foundation President Peter Perlman of the Peter Perlman Law Offices in Lexington, Kentucky. "Dozens of people were killed or maimed before

See Frankl, page 8.

Conference, San Antonio, Tx, November 2002

-----Original Message-----
From: CPhil49401@aol.com [mailto:CPhil49401@aol.com]
Sent: Sunday, April 01, 2007 10:39 AM
To: Coblio, Nicholas A.
Subject: Re: Tablet Splitting

Nick,

Why is this single pill splitting not mentioned in the VA research articles? Others copy pill splitting without this fundamental precaution.

Did you save the application to do research and the patient consent sheet? Do you have a safety paper to hand out now? (My home fax is 559-322-5307.)

Tampa must be the center of the largest of the VISN groups. Did Dr. Parra have his group use the same daily split to create a two day supply?

Do you think that the common pill doubling is much of a problem as the patient runs out of time to split for the day and tries to cover the dosing with one pill for two days? I seen the 2006 TIPS article where there have been 442 errors so far, mostly the double dose. One hospitalization /no death so far.

Chuck

In a message dated 4/1/2007 7:00:37 A.M. Pacific Daylight Time, Nicholas.Coblio@va.gov writes:

Hello:

Yes, the recommended procedure was, and still is, to split only one tablet at a time and take the next dose from the remains of the first split tablet. We use this procedure for any split doses.

Regards
-Nick
Nicholas A. Coblio, MSEM, PhD(abd), RPh
Pharmacy (119)
James A Haley VAH
Manager Pharmacy Quality/Information Management Systems
813 978-5804

-----Original Message-----
From: cphil49401@aol.com [mailto:cphil49401@aol.com]
Sent: Friday, March 30, 2007 9:08 PM
To: Coblio, Nicholas A.
Subject: Tablet Splitting

Dr. Coblio,

I have recently read the 2004 article "Using a Data Warehouse to Monitor Clinical Outcomes Associated with Simvasting Tablet Splitting." I am wondering if during the research you used the approach recommended by the Medical Letter (2004) of having the veteran split the tablet every

VA Florida